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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: _____ Examiner # : _____ Date: _____
Art Unit: _____ Phone Number 30_____ Serial Number: _____
Mail Box and Bldg Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

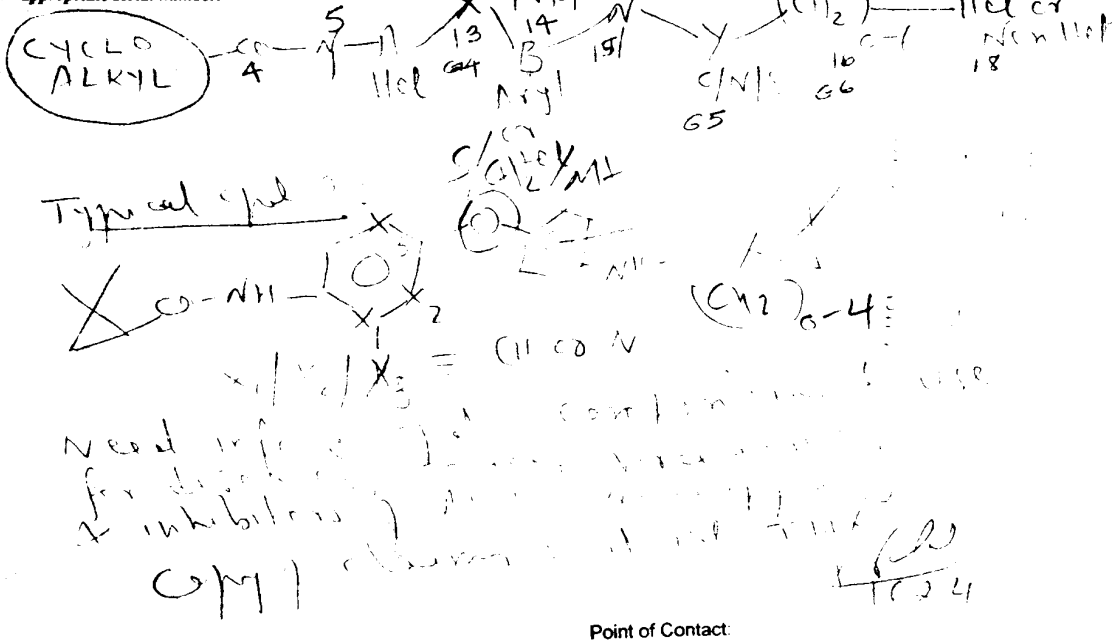
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: HETEROCYCLIC COMPOUNDS AND MEDICAL USE THEREOF

Inventors (please provide full names): YUKIO [illegible]

Earliest Priority Filing Date: 7/1/1997

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



Point of Contact:
Beverly Shears
Technical Info. Specialist
CM1 1E05 Tel: 308-4994

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: _____	NA Sequence (#)	STN
Searcher Phone # _____	AA Sequence (#)	Dialog
Searcher Location _____	Structure (#)	Questel Orbit
Date Searcher Picked Up _____	Bibliographic	Dr Link
Date Completed 5/5	Litigation	Lexis Nexis
Searcher Prep & Review Time 25	Fulltext	Sequence Systems
Clerical Prep Time _____	Patent Family	WWW Internet
Online Time 2.2	Other	Other (specify)

PTO-1590 (8-01)

L8 ANSWER 81 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1984:466008 CAPLUS
DN 101:66008
TI Modulating the immune response system in mammals
IN Lang, Stanley Albert, Jr.; Fields, Thomas Lynn; Wilkinson, Raymond George; Kang, Soon Mok; Lin, Yank I.
PA American Cyanamid Co., USA
SO Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 102476	A1	19840314	EP 1983-106543	19830705
	EP 102476	B1	19861105		

R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE

Patel

<5/3//2003>

			US 1982-405666	19820806
			US 1982-411399	19820825
US 4532349	A	19850730	US 1983-500715	19830603
			US 1982-411399	19820825
AT 23268	E	19861115	AT 1983-106543	19830705
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			US 1982-411399	19820825
			EP 1983-106543	19830705
JP 59046261	A2	19840315	JP 1983-142664	19830805
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ES 524772	A1	19850601	ES 1983-524772	19830805
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			US 1982-411399	19820825
CA 1215990	A1	19861230	CA 1983-433977	19830805
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			US 1982-411399	19820825
CA 1230057	A2	19871208	CA 1986-513549	19860710
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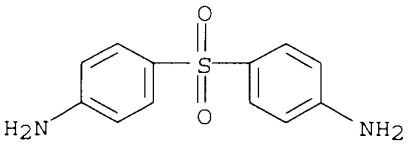
			US 1982-411399	19820825
			CA 1983-433977	19830805

OS CASREACT 101:66008

IT **80-08-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of, with chloroacetyl chloride)

RN 80-08-0 CAPLUS

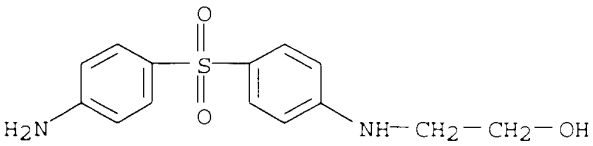
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



IT **80-02-4 565-20-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(immune adjuvant activity of, neoplasm treatment in relation to)

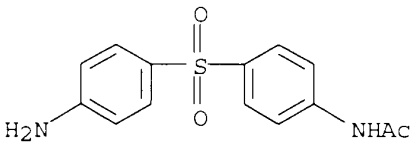
RN 80-02-4 CAPLUS

CN Ethanol, 2-[[4-[(4-aminophenyl)sulfonyl]phenyl]amino]- (9CI) (CA INDEX NAME)

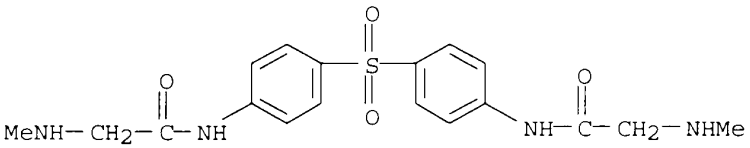


RN 565-20-8 CAPLUS

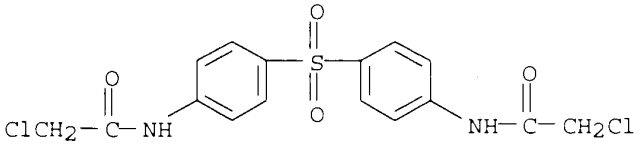
CN Acetamide, N-[4-[(4-aminophenyl)sulfonyl]phenyl]- (9CI) (CA INDEX NAME)



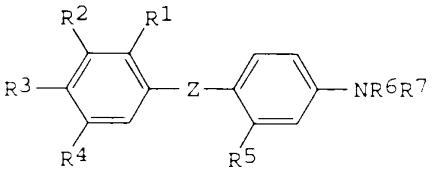
IT **32794-92-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and immune adjuvant activity of, neoplasm treatment in relation to)
RN 32794-92-6 CAPLUS
CN Acetamide, N,N'-(sulfonyldi-4,1-phenylene)bis[2-(methylamino)- (9CI) (CA INDEX NAME)



IT **17328-16-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction with methylamine)
RN 17328-16-4 CAPLUS
CN Acetamide, N,N'-(sulfonyldi-4,1-phenylene)bis[2-chloro- (9CI) (CA INDEX NAME)



GI



I

AB The prepn. of N-substituted phenylthioanilines, phenylsulfinylanilines,

and phenylsulfanylanilines I (R1 = H, Cl, or NO2; R2 = H or Cl; R3 = H, Br, Cl,Fl, NO2, C1-3 alkoxy, etc.; R4 and R5 = H or Cl; R6 = H or C1-3 alkyl; R7 = H, C1-3 alkyl, etc.; Z = S, SO, or SO2) is described for use as immune adjuvants. Some of the compds. were active in restoring antibody formation in mice with Rauscher virus-induced leukemia. The compds. may be useful for restoring immune function in **cancer**.

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 19	APOLLIT offering free connect time in April 2003
NEWS 28	Mar 20	EVENTLINE will be removed from STN
NEWS 29	Mar 24	PATDPAFULL now available on STN
NEWS 30	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 31	Apr 11	Display formats in DGENE enhanced
NEWS 32	Apr 14	MEDLINE Reload
NEWS 33	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 34	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 35	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 36	Apr 28	RDISCLOSURE now available on STN

NEWS EXPRESS	April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS	STN Operating Hours Plus Help Desk Availability

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 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *



FILE 'HOME' ENTERED AT 12:56:15 ON 03 MAY 2003

=> le reg
LE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 12:56:32 ON 03 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    2 MAY 2003  HIGHEST RN 509953-09-7
DICTIONARY FILE UPDATES:   2 MAY 2003  HIGHEST RN 509953-09-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
```

conducting SmartSELECT searches.

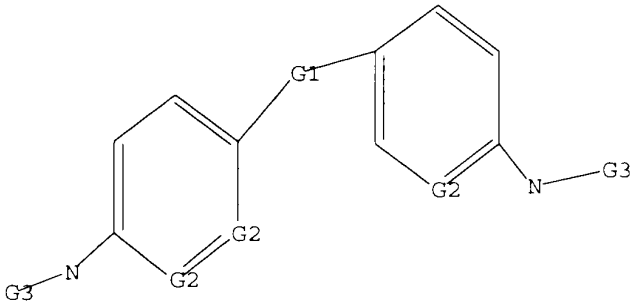
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 10029871.2

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 S,O,CH2,CH,SO2,NH

G2 C,S

G3 C,H

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 12:56:52 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 14260 TO ITERATE

7.0% PROCESSED 1000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 278057 TO 292343
PROJECTED ANSWERS: 32842 TO 37886

L2 50 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 12:57:00 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 287603 TO ITERATE

100.0% PROCESSED 287603 ITERATIONS 34596 ANSWERS
SEARCH TIME: 00.00.04

L3 34596 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 148.15 148.36

FILE 'CAPLUS' ENTERED AT 12:57:21 ON 03 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 3 May 2003 VOL 138 ISS 19
FILE LAST UPDATED: 2 May 2003 (20030502/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 40472 L3

=>

=> s l4 and AP-1
L5 2 L4 AND AP-1

=> s l4 and NF-Kappa
L6 4 L4 AND NF-KAPPA

=> s l4 and L5 and L6
L7 1 L4 AND L5 AND L6

=> d l6 fbib hitstr abs total

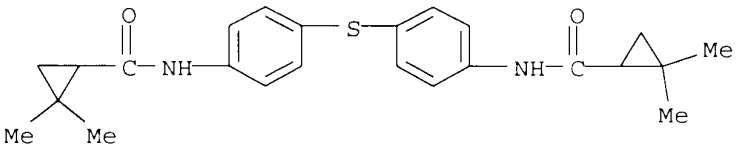
L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 2002:521476 CAPLUS
DN 137:73286
TI Preventives for wound adhesion
IN Kobayashi, Tsuyoshi; Konishi, Atsushi; Yuzawa, Kenji; Takehana, Kenji; Iino, Yukio
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2

DT Patent
LA Japanese
FAN.CNT 1

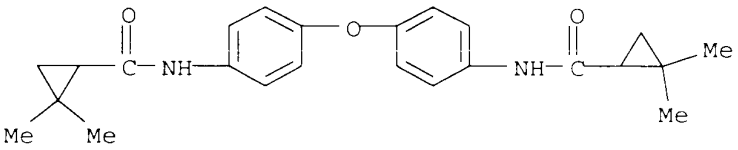
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002053150	A1	20020711	WO 2001-JP11202	20011220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
JP 2000-398133 A 20001227

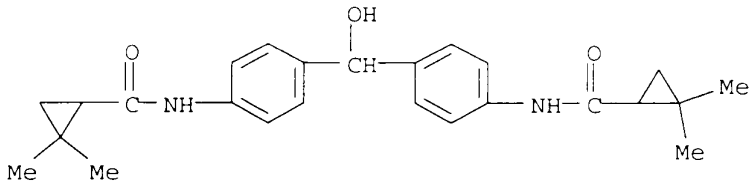
OS MARPAT 137:73286
IT **261001-11-0P 261001-13-2P 261001-19-8P**
261001-33-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclopropanecarboxamides as wound adhesion inhibitors)
RN 261001-11-0 CAPLUS
CN Cyclopropanecarboxamide, N,N'-(thiodi-4,1-phenylene)bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



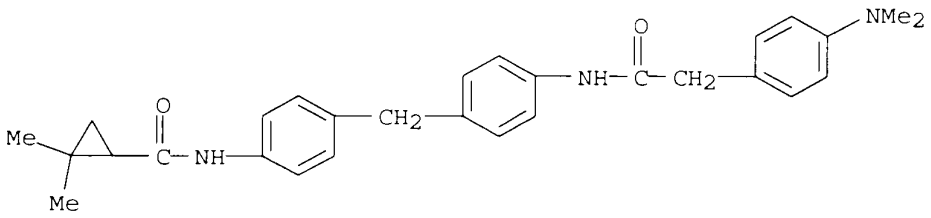
RN 261001-13-2 CAPLUS
CN Cyclopropanecarboxamide, N,N'-(oxydi-4,1-phenylene)bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



RN 261001-19-8 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[(hydroxymethylene)di-4,1-phenylene]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



RN 261001-33-6 CAPLUS
CN Benzeneacetamide, 4-(dimethylamino)-N-[4-[[4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]phenyl]methyl]phenyl]- (9CI) (CA INDEX NAME)



AB Disclosed are preventives for wound adhesion contg. specific cyclopropanecarboxylic acid amide compds. or pharmaceutically acceptable salts thereof which are efficacious in preventing wound adhesion. (1S)-N-[6-[4-[[[(1R)-2,2-dimethylcyclopropyl]carbonyl]amino]phenoxy]-3-pyridinyl]-2,2-dimethylcyclopropanecarboxamide (I) was prepd. and tested for its inhibitory activities against **NF**.**kappa**.B. I was also effective for preventing cell adhesion in kidney-transplanted Rhesus monkey.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 2001:338762 CAPLUS
DN 134:362292
TI Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
IN Farr, Spencer
PA Phase-1 Molecular Toxicology, USA
SO PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001032928	A2	20010510	WO 2000-US30474	20001103
	WO 2001032928	A3	20020725		

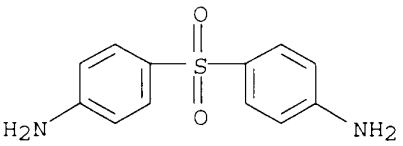
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 1999-165398PP 19991105
US 2000-196571PP 20000411

IT **80-08-0**, Dapsone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

RN 80-08-0 CAPLUS

CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS

AN 2001:12273 CAPLUS

DN 134:86271

TI Preparation of pyrimidine derivatives as Src-family protein tyrosine kinase inhibitor compounds

IN Armstrong, Helen M.; Beresis, Richard; Goulet, Joung L.; Holmes, Mark A.; Hong, Xingfang; Mills, Sander G.; Parsons, William H.; Sinclair, Peter J.; Steiner, Mark G.; Wong, Frederick; Zaller, Dennis M.

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 470 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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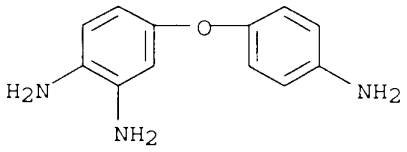
PI WO 2001000213 A1 20010104 WO 2000-US17443 20000626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 1999-141639PP 19990630
EP 1206265 A1 20020522 EP 2000-941701 20000626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
US 1999-141639PP 19990630
WO 2000-US17443W 20000626
US 6498165 B1 20021224 US 2000-604305 20000626
US 1999-141639PP 19990630

OS MARPAT 134:86271

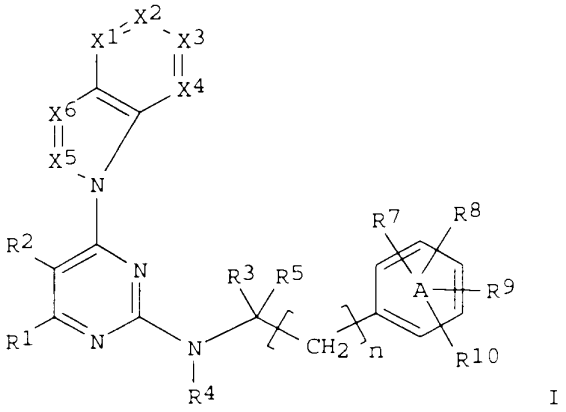
IT **6264-66-0**, 3,4,4'-Triaminodiphenyl ether
RL: RCT (Reactant); RACT (Reactant or reagent)
(for prepn. of pyrimidine derivs. as Src-family protein tyrosine kinase inhibitor compds.)

RN 6264-66-0 CAPLUS

CN 1,2-Benzenediamine, 4-(4-aminophenoxy)- (9CI) (CA INDEX NAME)



GI



I

AB What are claimed are pyrimidine compds. (shown as I), or their

pharmaceutically acceptable salts, hydrates, solvates, crystal forms and individual diastereomers, and pharmaceutical compns. including the same and their use as inhibitors of tyrosine kinase enzymes and consequently their use in the prophylaxis and treatment of protein tyrosine kinase-assocd. disorders, such as immune diseases, hyperproliferative disorders and other diseases in which inappropriate protein kinase action is believed to play a role, such as cancer, angiogenesis, atherosclerosis, graft rejection, rheumatoid arthritis and psoriasis. In I, R1, R2 = independently H, halo, OH, SH, CN, NO2, alkyl, alkoxy, acyloxy, alkoxycarbonyloxy, carbamoyloxy, alkylthio, sulfinyl, sulfonyl, acyl, alkoxycarbonyl, carbamoyl, amino, acylamino, ureido, sulfamoyl, sulfonylamino, or R1 and R2 can join together to form a fused methylenedioxy ring or a fused 6-membered arom. ring; terms such as 'alkyl' here and below are further defined in the claims. R3, R5 = independently H, C1-C6-alkyl unsubstituted or substituted with 1-3 substituents, aryl, or R3 and R5 taken together can represent :O; R3 or R5 can represent a 2 or 3 C methylene bridge forming a ring of 5-8 atoms fused to the A ring. R4 = H, C1-C6-alkyl, C1-C6-alkoxyl. X1, X2, X3, X4 in -X1:X2-X3:X4- are substituted or unsubstituted CH or N where 0-2 of X1, X2, X3, X4 are N. X5, X6 = independently N, C, optionally substituted CH. A ring = Ph, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, furanyl, benzothienyl, benzofuranyl, indolyl, imidazolyl, benzimidazolyl, thiadiazolyl. R7, R8, R9, R10 = independently H, halo, OH, SH, CN, NO2, N3, N2+BF4-, alkyl, alkoxy, alkylthio, sulfinyl, sulfonyl, C1-C6-alkyl, C1-C6-perfluoroalkyl, acyl, alkoxycarbonyl, carbamoyl, acyloxy, alkoxycarbonyloxy, carbamoyloxy, amino, acylamino, ureido, sulfamoyl, sulfonylamino, two of R7, R8, R9, and R10 when on adjacent carbons join together to form a methylenedioxy bridge. N = 0-2. More than 500 example prepns. are given, but no preparative method is claimed and no data relating to the usefulness of the compds. are given.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 2000:191054 CAPLUS
DN 132:222342
TI Benzene derivatives and medicinal use thereof
IN Iino, Yukio; Fujita, Kohichi; Tsuji, Takashi; Kodaira, Ariko; Takehana, Kenji; Kobayashi, Tsuyoshi; Yamamoto, Takashi
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000015603	A1	20000323	WO 1999-JP4986	19990913

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

				JP 1998-257804 A 19980911
	CA 2343101	AA	20000323	CA 1999-2343101 19990913
				JP 1998-257804 A 19980911
				WO 1999-JP4986 W 19990913
	AU 9956502	A1	20000403	AU 1999-56502 19990913
				JP 1998-257804 A 19980911
				WO 1999-JP4986 W 19990913
	BR 9913562	A	20010522	BR 1999-13562 19990913
				JP 1998-257804 A 19980911
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	EP 1113000	A1	20010704	EP 1999-943309 19990913
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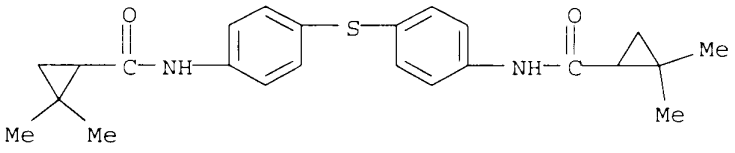
				JP 1998-257804 A 19980911
				WO 1999-JP4986 W 19990913
	NO 2001001157	A	20010425	NO 2001-1157 20010307
				JP 1998-257804 A 19980911
				WO 1999-JP4986 W 19990913
	US 2001018441	A1	20010830	US 2001-803107 20010312
				JP 1998-257804 A 19980911
				WO 1999-JP4986 A119990913

OS MARPAT 132:222342

IT **261001-11-0P 261001-17-6P 261001-19-8P 261001-23-4P 261001-24-5P 261001-25-6P 261001-27-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of benzene derivs. as medicine)

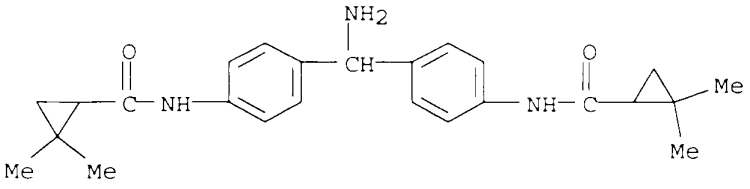
RN 261001-11-0 CAPLUS

CN Cyclopropanecarboxamide, N,N'-(thiodi-4,1-phenylene)bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



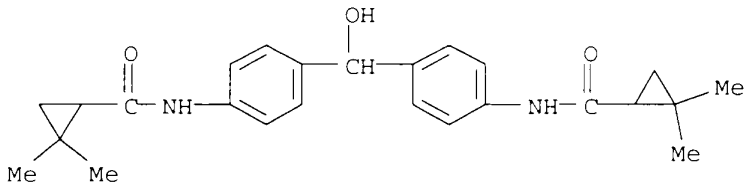
RN 261001-17-6 CAPLUS

CN Cyclopropanecarboxamide, N,N'-[(aminomethylene)di-4,1-phenylene]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)

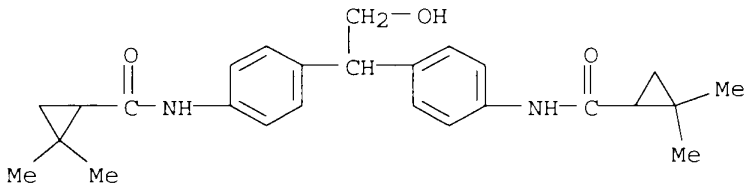


RN 261001-19-8 CAPLUS

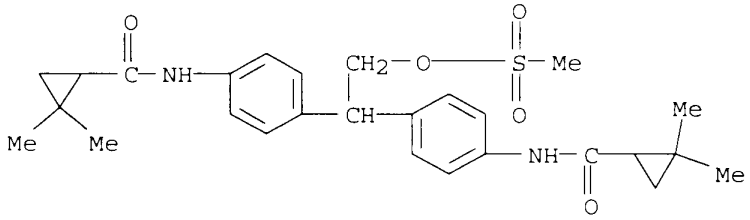
CN Cyclopropanecarboxamide, N,N'-[(hydroxymethylene)di-4,1-phenylene]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



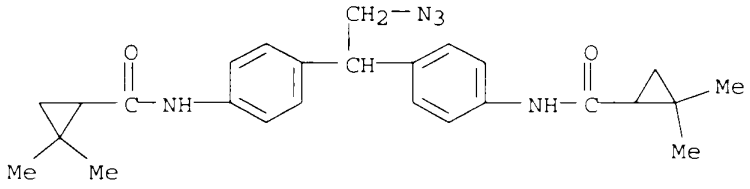
RN 261001-23-4 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[(2-hydroxyethylidene)di-4,1-phenylene]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



RN 261001-24-5 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[[2-[(methylsulfonyl)oxy]ethylidene]di-4,1-phenylene]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)

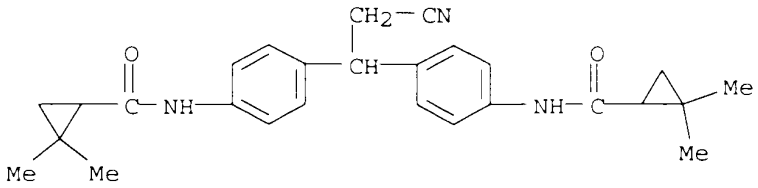


RN 261001-25-6 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[(2-azidoethylidene)di-4,1-phenylene]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



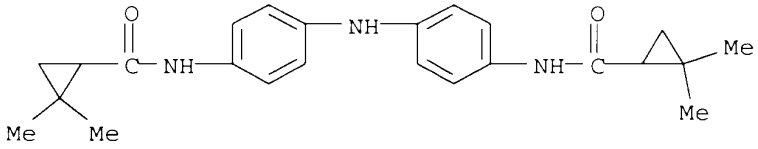
RN 261001-27-8 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[(2-cyanoethylidene)di-4,1-phenylene]bis[2,2-

dimethyl- (9CI) (CA INDEX NAME)

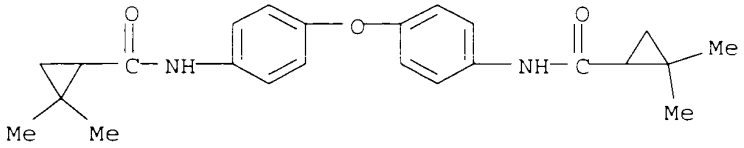


IT **261001-12-1P 261001-13-2P 261001-14-3P**
261001-18-7P 261001-20-1P 261001-21-2P
261001-26-7P 261001-28-9P 261001-31-4P
261001-32-5P 261001-33-6P 261001-34-7P
261001-35-8P 261001-36-9P 261001-42-7P
261001-43-8P 261001-46-1P 261001-51-8P
261001-52-9P 261001-53-0P 261001-63-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of benzene derivs. as medicine)

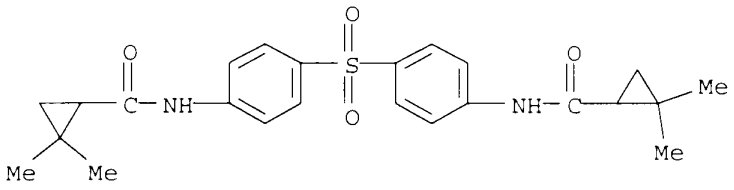
RN 261001-12-1 CAPLUS
CN Cyclopropanecarboxamide, N,N'-(iminodi-4,1-phenylene)bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



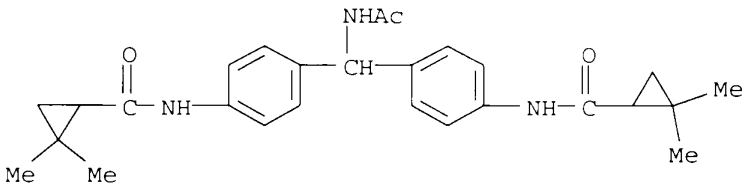
RN 261001-13-2 CAPLUS
CN Cyclopropanecarboxamide, N,N'-(oxydi-4,1-phenylene)bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



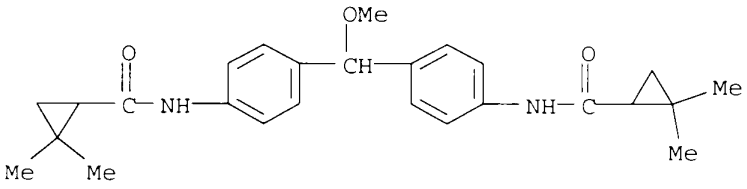
RN 261001-14-3 CAPLUS
CN Cyclopropanecarboxamide, N,N'-(sulfonyldi-4,1-phenylene)bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



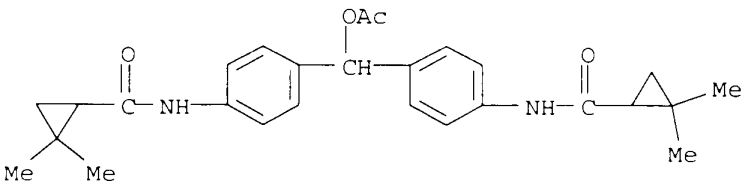
RN 261001-18-7 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[[(acetylamino)methylene]di-4,1-phenylene]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



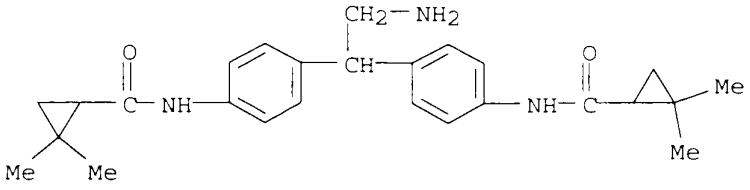
RN 261001-20-1 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[(methoxymethylene)di-4,1-phenylene]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



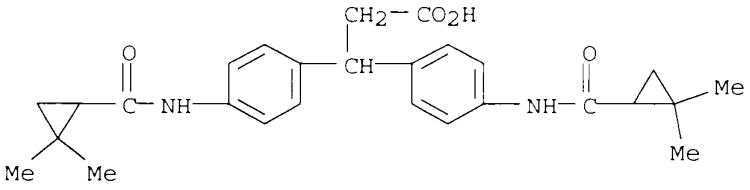
RN 261001-21-2 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[[(acetyloxy)methylene]di-4,1-phenylene]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



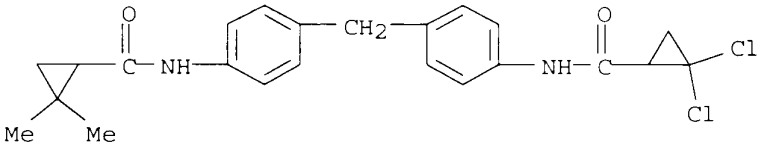
RN 261001-26-7 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[(2-aminoethylidene)di-4,1-phenylene]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



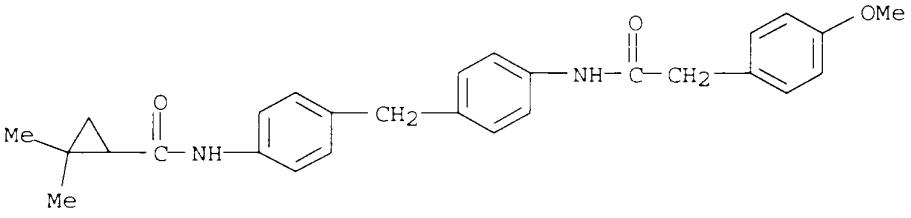
RN 261001-28-9 CAPLUS
CN Benzenepropanoic acid, 4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]-.beta.-[4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]phenyl]- (9CI) (CA INDEX NAME)



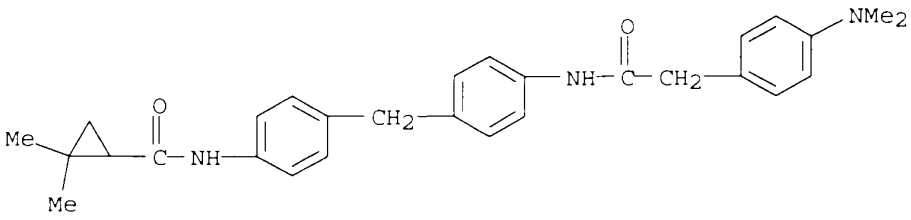
RN 261001-31-4 CAPLUS
CN Cyclopropanecarboxamide, N-[4-[[4-[[(2,2-dichlorocyclopropyl)carbonyl]amino]phenyl]methyl]phenyl]-2,2-dimethyl- (9CI) (CA INDEX NAME)



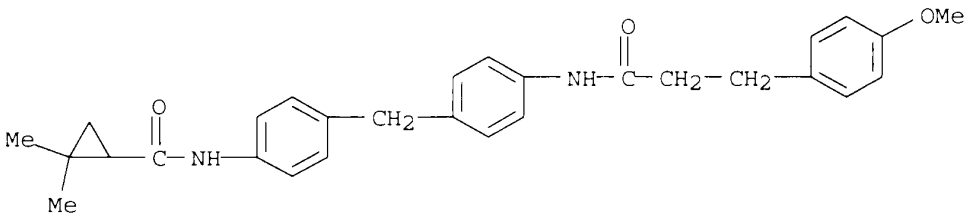
RN 261001-32-5 CAPLUS
CN Benzeneacetamide, N-[4-[[4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]phenyl]methyl]phenyl]-4-methoxy- (9CI) (CA INDEX NAME)



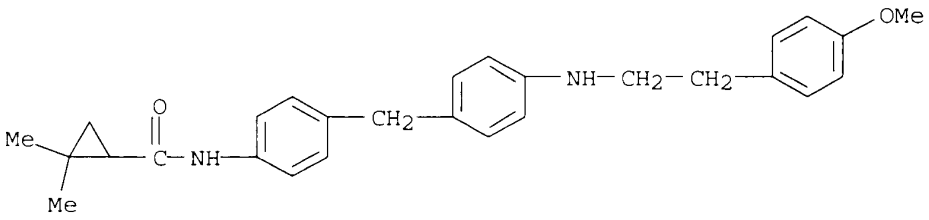
RN 261001-33-6 CAPLUS
CN Benzeneacetamide, 4-(dimethylamino)-N-[4-[[4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]phenyl]methyl]phenyl]- (9CI) (CA INDEX NAME)



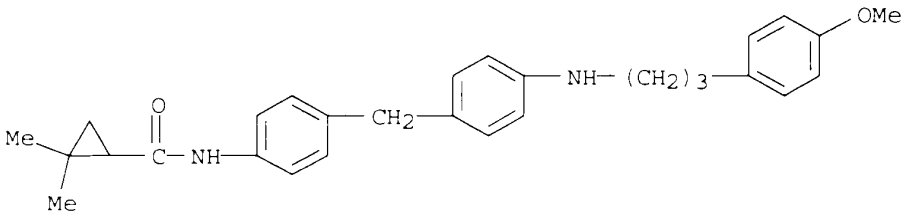
RN 261001-34-7 CAPLUS
CN Benzenepropanamide, N-[4-[[4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]phenyl]methyl]phenyl]-4-methoxy- (9CI) (CA INDEX NAME)



RN 261001-35-8 CAPLUS
CN Cyclopropanecarboxamide, N-[4-[[4-[[2-(4-methoxyphenyl)ethyl]amino]phenyl]methyl]phenyl]-2,2-dimethyl- (9CI) (CA INDEX NAME)

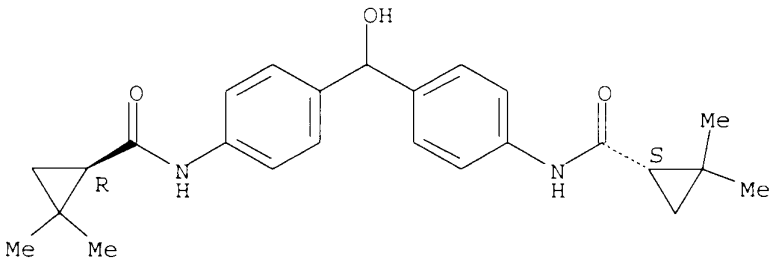


RN 261001-36-9 CAPLUS
CN Cyclopropanecarboxamide, N-[4-[[4-[[3-(4-methoxyphenyl)propyl]amino]phenyl]methyl]phenyl]-2,2-dimethyl- (9CI) (CA INDEX NAME)



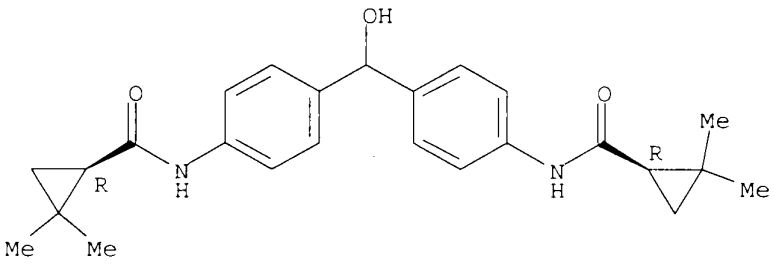
RN 261001-42-7 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[(hydroxymethylene)di-4,1-phenylene]bis[2,2-dimethyl-, (1R,1'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

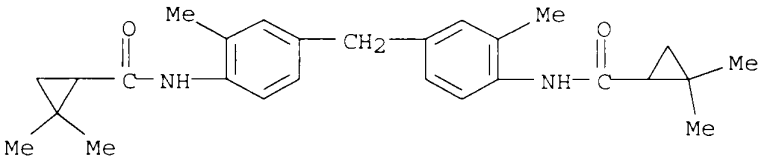


RN 261001-43-8 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[(hydroxymethylene)di-4,1-phenylene]bis[2,2-dimethyl-, (1R,1'R)- (9CI) (CA INDEX NAME)

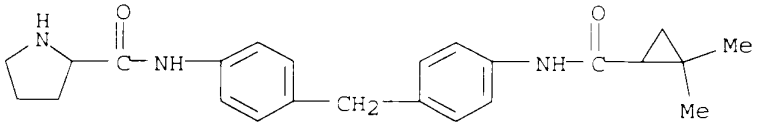
Absolute stereochemistry.



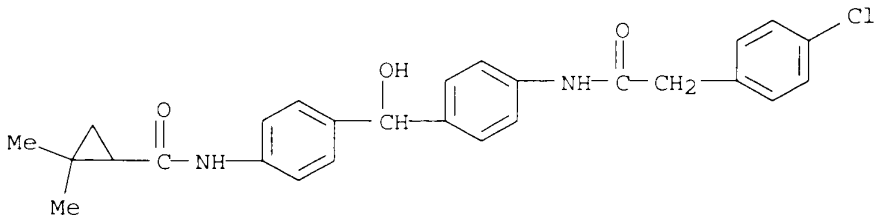
RN 261001-46-1 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[methylenebis(2-methyl-4,1-phenylene)]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



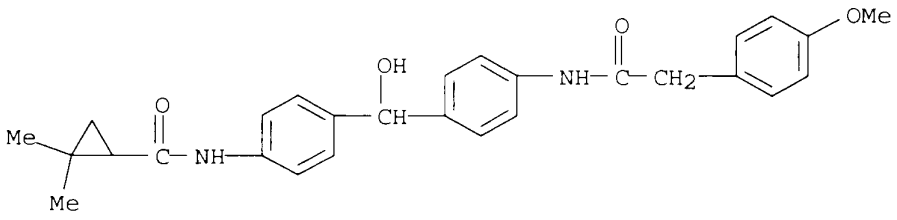
RN 261001-51-8 CAPLUS
CN 2-Pyrrolidinecarboxamide, N-[4-[[4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]phenyl]methyl]phenyl]- (9CI) (CA INDEX NAME)



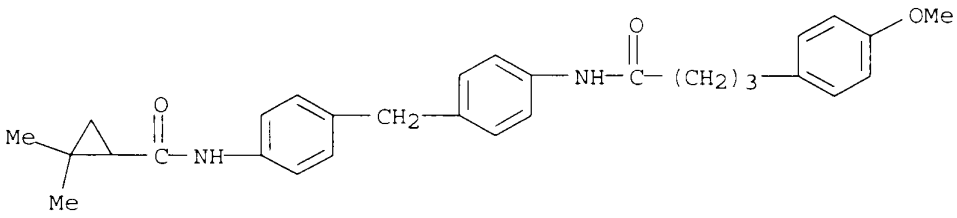
RN 261001-52-9 CAPLUS
CN Benzeneacetamide, 4-chloro-N-[4-[[4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]phenyl]hydroxymethyl]phenyl]- (9CI) (CA INDEX NAME)



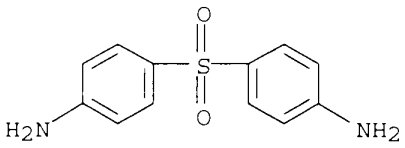
RN 261001-53-0 CAPLUS
CN Benzeneacetamide, N-[4-[[4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]phenyl]hydroxymethyl]phenyl]-4-methoxy- (9CI) (CA INDEX NAME)



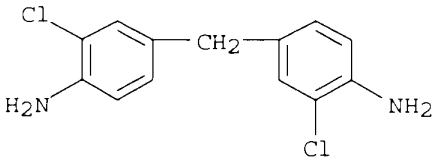
RN 261001-63-2 CAPLUS
CN Benzenebutanamide, N-[4-[[4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]phenyl]methyl]phenyl]-4-methoxy- (9CI) (CA INDEX NAME)



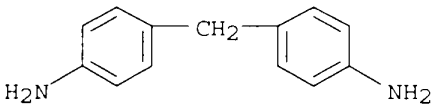
IT **80-08-0 101-14-4 101-77-9 101-80-4**
139-65-1, 4,4'-Diaminodiphenylsulfide **838-88-0**
4073-98-7 53760-27-3, 4,4'-Diaminodiphenylamine sulfate
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of benzene derivs. as medicine)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



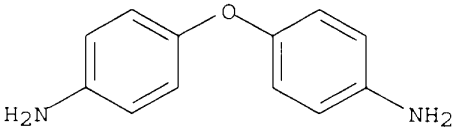
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



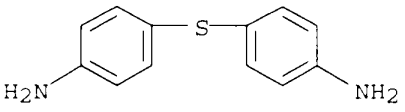
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



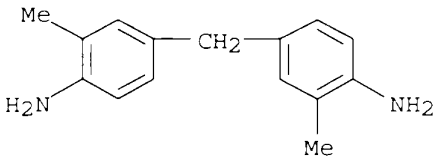
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



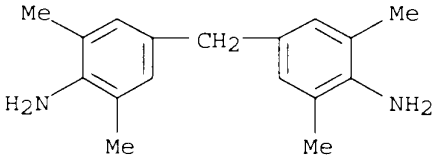
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



RN 838-88-0 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-methyl- (9CI) (CA INDEX NAME)



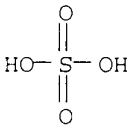
RN 4073-98-7 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2,6-dimethyl- (9CI) (CA INDEX NAME)



RN 53760-27-3 CAPLUS
CN 1,4-Benzenediamine, N-(4-aminophenyl)-, sulfate (1:1) (9CI) (CA INDEX NAME)

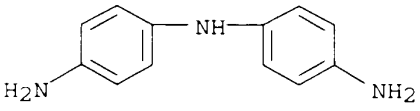
CM 1

CRN 7664-93-9
CMF H2 O4 S

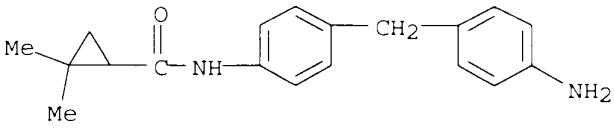


CM 2

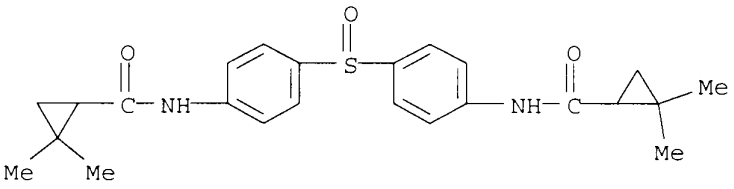
CRN 537-65-5
CMF C12 H13 N3



IT **261001-30-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of benzene derivs. as medicine)
RN 261001-30-3 CAPLUS
CN Cyclopropanecarboxamide, N-[4-[(4-aminophenyl)methyl]phenyl]-2,2-dimethyl- (9CI) (CA INDEX NAME)

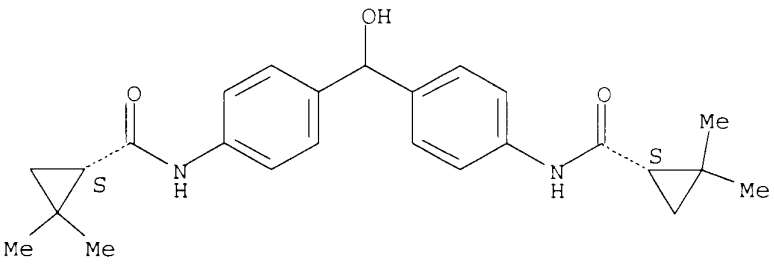


IT **261001-29-0P 261001-41-6P 261001-45-0P**
261001-47-2P 261001-61-0P 261001-62-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of benzene derivs. as medicine)
RN 261001-29-0 CAPLUS
CN Cyclopropanecarboxamide, N,N'-(sulfinyldi-4,1-phenylene)bis[2,2-dimethyl- (9CI) (CA INDEX NAME)

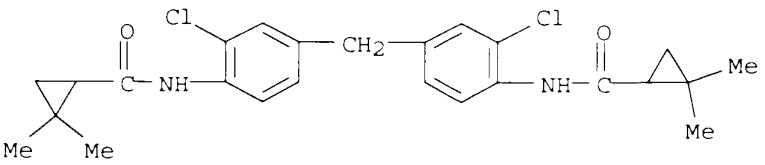


RN 261001-41-6 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[(hydroxymethylene)di-4,1-phenylene]bis[2,2-dimethyl-, (1S,1'S)- (9CI) (CA INDEX NAME)

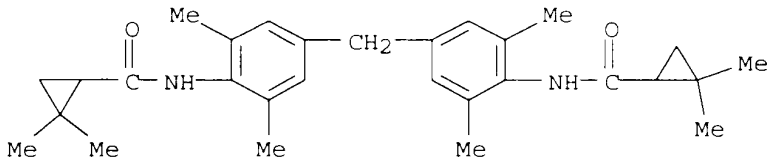
Absolute stereochemistry.



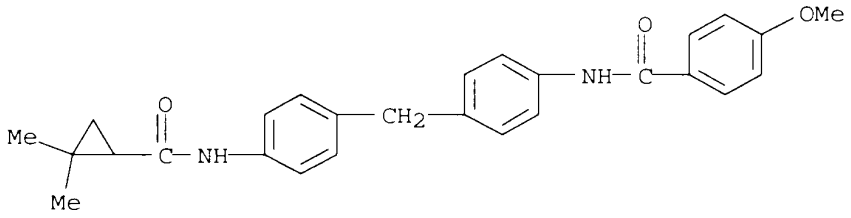
RN 261001-45-0 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[methylenebis(2-chloro-4,1-phenylene)]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



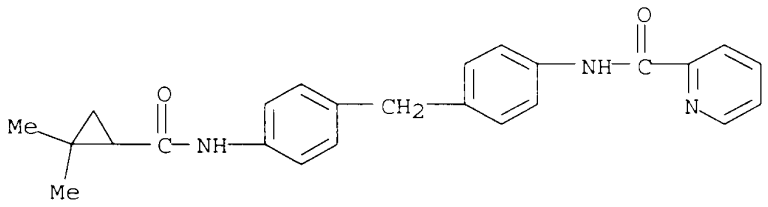
RN 261001-47-2 CAPLUS
CN Cyclopropanecarboxamide, N,N'-[methylenebis(2,6-dimethyl-4,1-phenylene)]bis[2,2-dimethyl- (9CI) (CA INDEX NAME)



RN 261001-61-0 CAPLUS
CN Benzamide, N-[4-[[4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]phenyl]methyl]phenyl]-4-methoxy- (9CI) (CA INDEX NAME)



RN 261001-62-1 CAPLUS
CN 2-Pyridinecarboxamide, N-[4-[[4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]phenyl]methyl]phenyl]- (9CI) (CA INDEX NAME)



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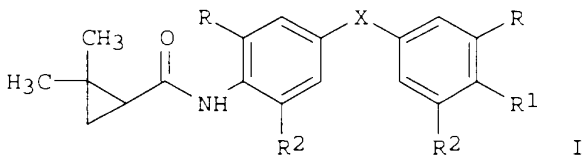

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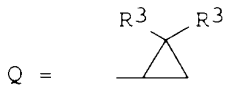

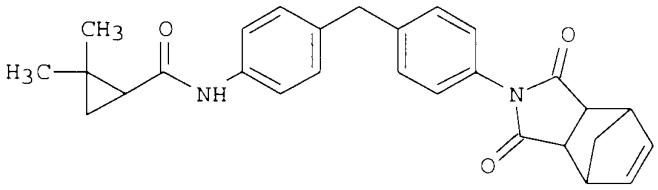

II

AB Title compds. [I; X = CO, S, NH, O, SO2, CH2, CH2CH2, CHOH, CHOCH3, C:CH2, CHCH2OH, S:O, OCH2, SCH2, CH:CH, SO2NH, SO2NCH3, CONH, CONCH3; R = H, CH3, Cl; R1 = NHCOQ, 4-CH3OC6H4CH2CONH, 4-CH3OC6H4CH2CH2CH2NH, 4-CH3OC6H4CH2CH2CONH, NH2, 4(CH3)2NC6H4CH2CONH, 4-ClC6H4CH2CONH, NHCOCH3; R3 = Cl, CH3; Q = N-contg.-heterocyclo], stereoisomers, and pharmaceutically acceptable salts thereof are prepd. as AP-1 activation inhibitors, **NF-kappa** B activation inhibitors, inflammatory cytokine prodn. inhibitors, matrix metalloprotease prodn. inhibitors, inflammatory cell adhesion factor expression inhibitors, anti-inflammatory agents, antirheumatic agents, immunosuppressive agents, cancerous metastasis inhibitors, and remedies for arteriosclerosis or antiviral agents contg. the above compds. as the active ingredient. The title compd. II was prepd. and tested.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

=> d his

(FILE 'HOME' ENTERED AT 12:56:15 ON 03 MAY 2003)

FILE 'REGISTRY' ENTERED AT 12:56:32 ON 03 MAY 2003
L1 STRUCTURE UPLOADED
L2 50 S L1
L3 34596 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 12:57:21 ON 03 MAY 2003
L4 40472 S L3

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L5            2 S L4 AND AP-1
L6            4 S L4 AND NF-KAPPA
L7            1 S L4 AND L5 AND L6

=> s l4 and cancer
L8          105 L4 AND CANCER

=> s l4 and viral disease
L9            1 L4 AND VIRAL DISEASE

=> d l9 fbib hitstr abs total

L9   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
AN   1963:59547  CAPLUS
DN   58:59547
OREF 58:10126h,10127a
TI   Bis(p-ureidophenyl) sulfones
PA   Chemie Gruenenthal G.m.b.H.
SO   18 pp.
DT   Patent
LA   Unavailable
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
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PI   FR M1489                19621015      FR
                                           DE               19600726
     DE 1164393                            DE
     GB 973900                             GB
IT   1260-11-3, Urea, 1,1'-(sulfonyldi-p-phenylene)bis[3-(4-pyridyl)-
     1261-46-7, Carbanilide, 4,4''-sulfonylbis[4'-hydroxythio-
     1262-82-4, Carbanilide, 4,4''-sulfonylbis[4'-nitro-
     1444-18-4, Carbanilide, 4,4''-sulfonylbis[4'-mercapto-
     3948-56-9, Carbanilide, 4,4''-sulfonylbis[4'-hydroxy-
     4234-56-4, Carbanilide, 4,4''-sulfonylbis[4'-acetylthio-
     98878-42-3, Carbanilide, 4,4''-sulfonylbis[4'-amino-
        (prepn. of)
RN   1260-11-3  CAPLUS
CN   Urea, 1,1'-(sulfonyldi-p-phenylene)bis[3-(4-pyridyl)- (7CI, 8CI)  (CA
     INDEX NAME)
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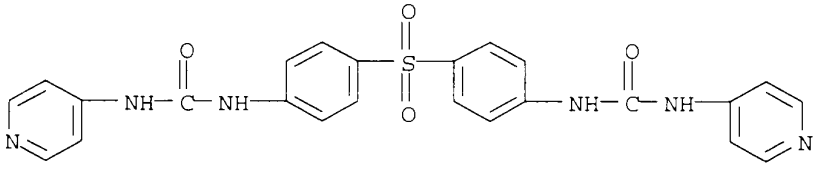

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CN   Carbanilide, 4,4''-sulfonylbis[4'-hydroxythio- (7CI, 8CI)  (CA INDEX NAME)
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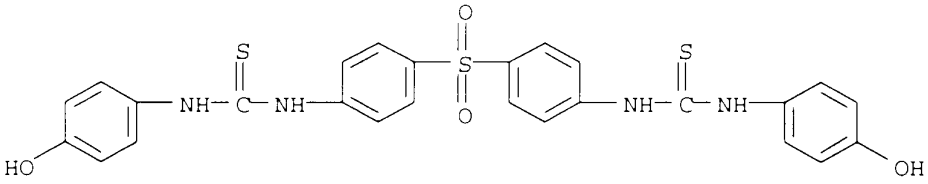
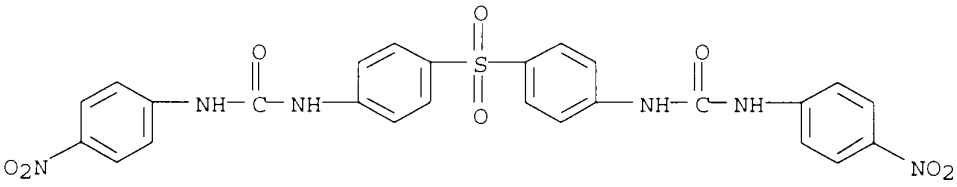
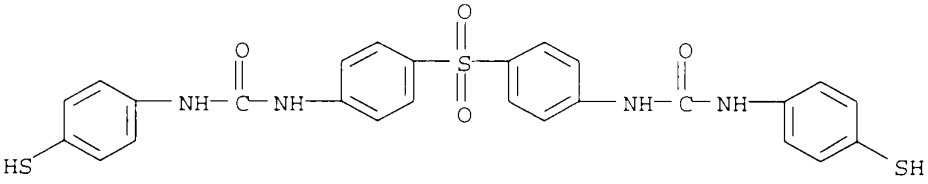


RN 1262-82-4 CAPLUS
CN Urea, N,N''-(sulfonyldi-4,1-phenylene)bis[N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



RN 1444-18-4 CAPLUS
CN Carbanilide, 4,4''-sulfonylbis[4'-mercapto- (7CI, 8CI) (CA INDEX NAME)



RN 3948-56-9 CAPLUS
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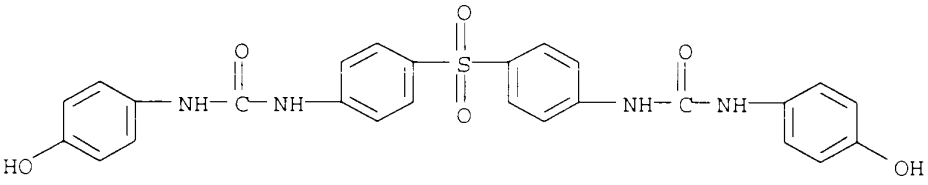
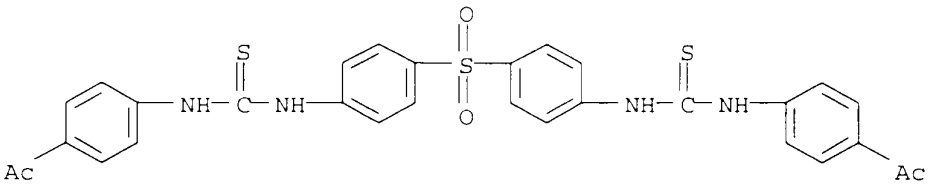


RN 4234-56-4 CAPLUS
CN Carbanilide, 4,4''-sulfonylbis[4'-acetylthio- (7CI, 8CI) (CA INDEX NAME)



RN 98878-42-3 CAPLUS
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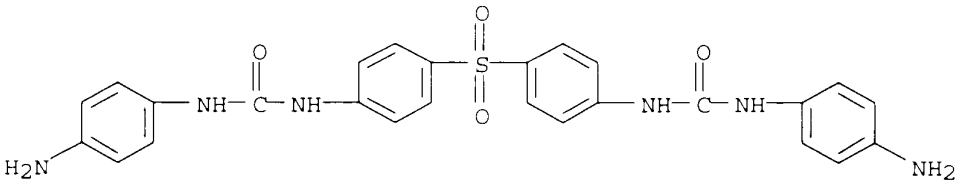

AB Compds. of the general formula [p-(RNHCONH)C6H4]2SO2 (I), in which R is a pyridyl or a substituted Ph group, can be used in the treatment of **viral diseases**. [p-(OCN)C6H4]2SO2(12.4 g.) in 370 ml. anhyd. dioxane is added to a warm soln. of 10.9 g. p-H2NC6H4OH in 370 ml. dry dioxane, the mixt. heated 1 hr., the ppt. filtered off, dissolved in iso-PrOH, and ether added to the soln. to give [p-[(p-HOC6H4)NHCONH]C6H4]2SO2, m. 188-90.degree. (decompn.), 84.8% yield. Similarly prepd. are compds. of the general formula I (R, m.p., yield given): p-O2NC6H4, 166.degree. (decompn.), 81.9%; p HSC6H4, 207-9.degree., 84%; 4-pyridyl, 188.degree., 76.3%; p-(n-BuO)C6H4, 156.degree., 53.8%; and p-H2NC6H4, --, 71.5%. Also prepd. are compds. of formula [p-(RNHCS-NH)C6H4]2SO2 (given R, m.p., yield): p-HOC6H4, 129.degree. (decompn.), 69.8% and p-AcC6H4, 159.degree. (decompn.), 72.4%.

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=> d his

     (FILE 'HOME' ENTERED AT 12:56:15 ON 03 MAY 2003)

     FILE 'REGISTRY' ENTERED AT 12:56:32 ON 03 MAY 2003
L1             STRUCTURE UPLOADED
L2              50 S L1
L3           34596 S L1 SSS FULL

     FILE 'CAPLUS' ENTERED AT 12:57:21 ON 03 MAY 2003
L4           40472 S L3
L5               2 S L4 AND AP-1
L6               4 S L4 AND NF-KAPPA
L7               1 S L4 AND L5 AND L6
L8             105 S L4 AND CANCER
L9               1 S L4 AND VIRAL DISEASE

=> d l8 fbib hitstr abs total

L8   ANSWER 1 OF 105  CAPLUS  COPYRIGHT 2003 ACS
AN   2003:202623  CAPLUS
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DN 138:230989
TI Preparation of cyclen-based chelates as multi-use multimodal imaging agents
IN Bornhop, Darryl J.; Manning, Charles H.; Goebel, Timothy
PA Texas Tech University, USA
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

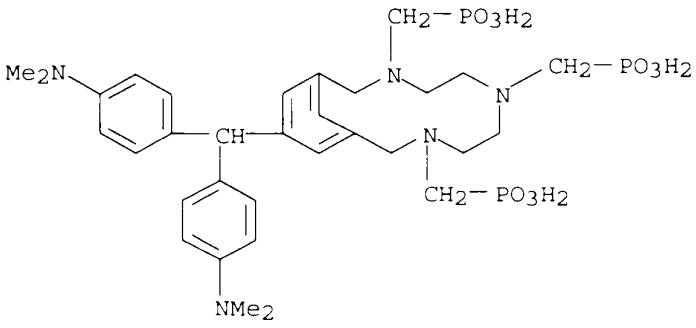
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003020701	A2	20030313	WO 2002-US27800	20020904

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

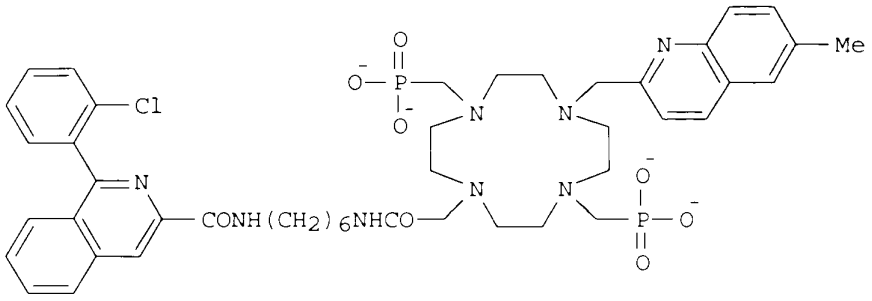
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-316284PP 20010904
US 2001-316303PP 20010904

OS MARPAT 138:230989
IT **501084-46-4DP**, lanthanide complexes
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclen-based chelates as multi-use multimodal contrast agents for fluorescence/MRI/CT/NIR/x-ray imaging)
RN 501084-46-4 CAPLUS
CN Phosphonic acid, [[13-[bis[4-(dimethylamino)phenyl]methyl]-3,6,9-triazabicyclo[9.3.1]pentadeca-1(15),11,13-triene-3,6,9-triyl]tris(methylene)]tris- (9CI) (CA INDEX NAME)



GI



I

AB Cyclen-based chelates can be used as contrast agents for multi-modal imaging of tissue cells. The cyclen-based chelates are preferably polyazamacrocyclic mols. formed from 1,4,7,10-tetraazacyclododecane (cyclen) having varying chelating ions, phosphoester chains, and light harvesting moieties. By changing the chelating ion, phosphoester chain length and/or the light harvesting moiety different imaging techniques, such as MRI, CT, fluorescence and absorption, x-ray and NIR, may be employed to image the tissue cells. Addnl., the cyclen-based chelates may be conjugated to provide for site-specific delivery of the cyclen-based chelate to the desired tissue cells. The cyclen-based chelates may also be delivered to the tissue cells by attaching the cyclen-based chelates to a polymeric delivery vehicle. Although these cyclen-based chelates have a wide variety of application, the preferred use is for imaging of **cancer** cells, such as brain **cancer**, for improving resection of a cancerous tissue. Thus, lanthanide chelates of cyclen deriv. (I) and related complexes were prepd. The use of europium complexes as fluorescent imaging agents and of gadolinium complexes as MRI contrast agents is discussed and demonstrated.

L8 ANSWER 2 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2002:946092 CAPLUS
DN 138:11401
TI Steroid hormone and nonsteroidal anti-inflammatory drug (NSAID) combinations for inducing tumor cell apoptosis
IN Andrews, Peter; Djakiew, Daniel
PA Georgetown University, USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

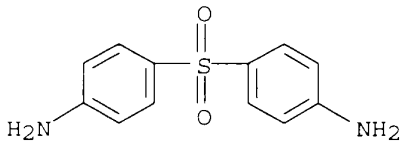
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002098403	A1	20021212	WO 2002-US17193	20020603

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-294583PP 20010601

IT **80-08-0**, Dapsone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(steroid hormone and nonsteroidal anti-inflammatory drug combination for inducing tumor cell apoptosis)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)

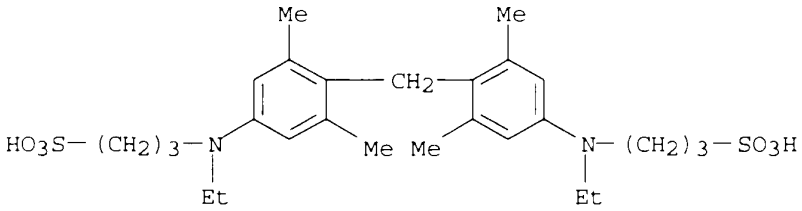


AB A pharmaceutical compn. is described, having at least one nonsteroidal anti-inflammatory drug (NSAID), at least one steroid hormone, a pharmaceutically acceptable carrier, and optionally, one or more excipients, wherein the at least one NSAID and the at least one steroid hormone are present in amts. sufficient to induce tumor cell apoptosis. Also described is a method of inducing apoptosis of **cancer** cells in which therapeutically effective amts. of at least one NSAID and at least one steroid hormone are administered to a subject. The NSAID and steroid hormone may administered prophylactically to a subject having nonmeasurable tumor burden, or may be administered to a subject having a detectable tumor.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2002:928122 CAPLUS
DN 138:12504
TI Method for assaying biomolecules and other constituents using indicator conjugates with synthetic nucleounits in lateral flow, liquid, and dry chemistry techniques
IN Smith, Jack V.
PA USA
SO U.S. Pat. Appl. Publ., 46 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

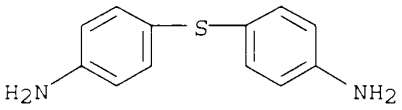
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002182600	A1	20021205	US 2001-829563	20010411
			US 2001-829563	20010411

IT **181066-50-2**, Bis-MAPS-C 2
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(indicator; method for assaying biomols. and other constituents using indicator conjugates with synthetic nucleounits in lateral flow, liq., and dry chem. techniques)
RN 181066-50-2 CAPLUS
CN 1-Propanesulfonic acid, 3,3'-[methylenebis[(3,5-dimethyl-4,1-phenylene)(ethylimino)]]bis- (9CI) (CA INDEX NAME)



AB The present invention is a method for the use of particles made up of nucleotides or fragments of base groups of DNA and RNA mols. herein referred to as synthetic nucleounits which can be used as recognition mols. with specificity and sensitivity significantly greater than that of antibodies which are used in clin. diagnostics, biotechnol., and research. The method for detecting an analyte using nucleounits targeted to the analyte comprises (1) identifying a nucleounit from a mixt. of synthetic random sequences of nucleounit libraries, (2) conjugating the nucleounit to an indicator for the analyte, and (3) detecting the analyte using the nucleounit-indicator conjugate in a buffer. Step 1 is carried out by (a) contacting the analyte with the mixt. of synthetic random sequences of nucleounit libraries such that some nucleounits bind the analyte, (b) removing the unbound nucleounits by partitioning, and (c) amplifying the remaining nucleounits by PCR to obtain an enriched soln. of nucleounits with high affinity for the analyte. Thus, a method and lateral flow test strip for detection of cytomegalovirus (CMV) presence in a biol. sample such as serum or urine is described. The strip is prepd. with three solns., one contg. anti-CMV antibodies, one contg. "nucleounit to CMV antibody conjugated to red microparticles" and "red microparticles", and another contg. "nucleounit to colored particles". The "nucleounit" may be an oligonucleotide aptamer specific for anti-CMV antibodies.

L8 ANSWER 4 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2002:835372 CAPLUS
DN 138:20798
TI Carcinogenic effect of combined administration of 2,4-diaminoanisole sulfate, 4,4'-thiodianiline and N,N'-diethylthiourea in male Wistar rats
AU Pomorski, L.; Bartos, M.; Okruszek, A.; Matejkowska, M.; Tazbir, J.; Kuzdak, K.
CS Clinic of Endocrinological and General Surgery, Institute of Endocrinology, Medical University of Lodz, 93-513, Pol.
SO Neoplasma (2002), 49(4), 247-250
CODEN: NEOLA4; ISSN: 0028-2685
PB VEDA
DT Journal
LA English
IT **139-65-1**, 4,4'-Thiodianiline
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(2,4-diaminoanisole sulfate, 4,4'-thiodianiline and N,N'-diethylthiourea in male Wistar rats carcinogenic effect after combined administration)
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



AB Male Wistar rats were divided into two groups. Rats of group 1 were fed basal powd. diet contg. 610 ppm 2,4-diaminoanisole sulfate (DAAS), 46 ppm 4,4'-thiodianiline (TDA) and 200 ppm N,N'-diethylthiourea (DETU) for 52 wk (DTD treatment). Rats of group 2 were maintained on basal diet throughout the expt. as controls. At 52 wk all surviving rats were sacrificed and subjected to an autopsy. Thyroid, lungs, stomach, liver, spleen, kidneys, testes and all gross lesions suspected of being a tumor were removed. After DTD treatment, the incidence of thyroid hyperplasia and papillary thyroid carcinoma was 59% (10/17) and 65% (11/17), resp. Hepatocellular adenoma was induced in 2 of 17 rats (12%). Papillary thyroid carcinoma metastasis was found in the lung of 1 rat. No neoplastic tumors were found in kidney, spleen, stomach and testis tissue.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2002:594624 CAPLUS
DN 137:150264
TI Benz-1,3-azole derivatives, their preparation, and their uses as heparanase inhibitors
IN Ayal-Hershkovitz, Maty; Miron, Daphna; Levy, Ofra
PA Insight Strategy and Marketing Ltd., Israel
SO PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

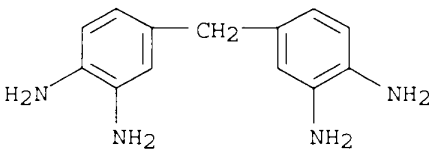
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002060374	A2	20020808	WO 2002-IL81	20020129
WO 2002060374	A3	20030227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

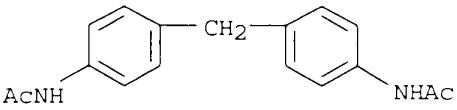
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-264306PP 20010129

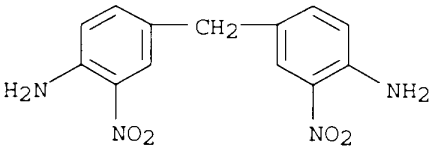
OS MARPAT 137:150264
IT **1779-05-1P 2719-05-3P 17474-44-1P**
19014-15-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; benz-1,3-azole deriv. prepn. and use as heparanase inhibitors)
RN 1779-05-1 CAPLUS
CN 1,2-Benzenediamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



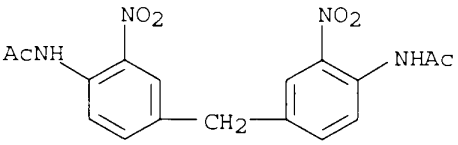
RN 2719-05-3 CAPLUS
CN Acetamide, N,N'-(methylenedi-4,1-phenylene)bis- (9CI) (CA INDEX NAME)



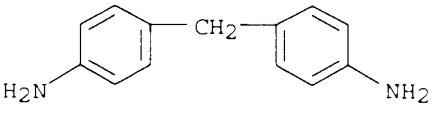
RN 17474-44-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-nitro- (9CI) (CA INDEX NAME)



RN 19014-15-4 CAPLUS
CN Acetamide, N,N'-[methylenebis(2-nitro-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)



IT **101-77-9**, 4,4'-Methylenedianiline
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; benz-1,3-azole deriv. prepn. and use as heparanase inhibitors)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



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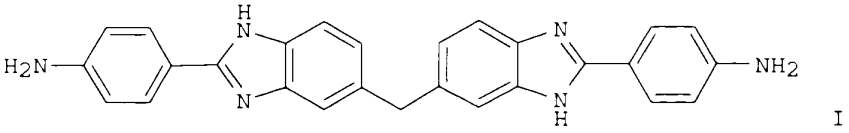
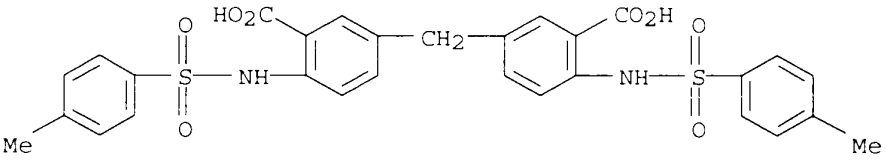


I

AB The invention provides benz-1,3-azole derivs., namely benzimidazole, benzoxazole and benzthiazole derivs. as heparanase inhibitors suitable for treatment of diseases and disorders caused by or assocd. with heparanase catalytic activity, e.g. **cancer**, inflammatory disorders, and autoimmune diseases. Prepn. and biol. activity of e.g. I are described.

L8 ANSWER 6 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2002:576360 CAPLUS
DN 138:231345
TI A small-molecule inhibitor of the ribonucleolytic activity of human angiogenin that possesses antitumor activity
AU Kao, Richard Y. T.; Jenkins, Jeremy L.; Olson, Karen A.; Key, Marc E.; Fett, James W.; Shapiro, Robert
CS Center for Biochemical and Biophysical Sciences and Medicine, Harvard Medical School, Cambridge, MA, 02139, USA
SO Proceedings of the National Academy of Sciences of the United States of America (2002), 99(15), 10066-10071
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
IT **501444-05-9**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(small-mol. inhibitor of ribonucleolytic activity of human angiogenin that possesses antitumor activity in human cells)
RN 501444-05-9 CAPLUS
CN Benzoic acid, 3,3'-methylenebis[6-[[(4-methylphenyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)



AB The results of previous preclin. and clin. studies have identified angiogenin (ANG) as a potentially important target for anticancer therapy. Here the authors report the design and implementation of a high-throughput screening assay to identify small mols. that bind to the ribonucleolytic active site of ANG, which is critically involved in the induction of angiogenesis by this protein. Screening of 18,310 compds. from the National **Cancer** Institute (NCI) Diversity Set and ChemBridge DIVERSet yielded 15 hits that inhibit the enzymic activity of ANG with Ki values <100 .mu.M. One of these, NCI compd. 65828 [8-amino-5-(4'-hydroxybiphenyl-4-ylazo)naphthalene-2-sulfonate; Ki = 81 .mu.M], was

selected for more detailed studies. Minor changes in ANG or ligand structure markedly reduced potency, demonstrating that inhibition reflects active-site rather than nonspecific binding: these observations are consistent with a computationally generated model of the ANG.cntdot.65828 complex. Local treatment with modest doses of 65828 significantly delayed the formation of s.c. tumors from two distinct human **cancer** cell types in athymic mice. ANG is the likely target involved because (i) a 65828 analog with much lower potency against the enzymic activity of ANG failed to exert any antitumor effect, (ii) tumors from 65828-treated mice had fewer interior blood vessels than those from control mice, and (ii) 65828 appears to have no direct effect on the tumor cells. The authors' findings provide considerable support for the targeting of the enzymic active site of ANG as a strategy for developing new anticancer drugs.

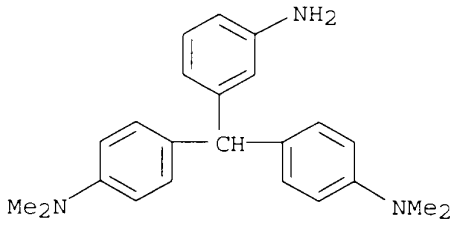
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2002:555348 CAPLUS
DN 137:124985
TI Preparation of triphenylmethanes as kinesin KSP inhibitors
IN Finer, Jeffrey T.; Chabala, John C.; Lewis, Evan
PA Cytokinetics, Inc., USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

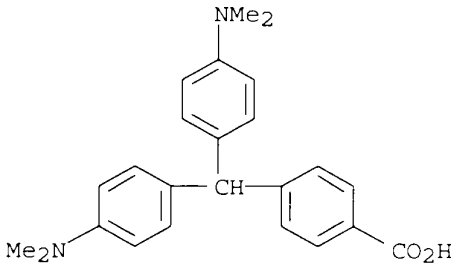
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002056880	A1	20020725	WO 2002-US1614	20020118

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2001-263015PP 20010119

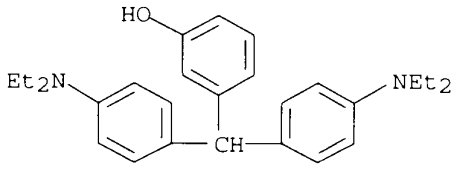
OS MARPAT 137:124985
IT **6258-99-7P 77290-43-8P 443893-62-7P**
443893-66-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of triphenylmethanes as kinesin KSP inhibitors)
RN 6258-99-7 CAPLUS
CN Benzenamine, 4,4'-[(3-aminophenyl)methylene]bis[N,N-dimethyl- (9CI) (CA INDEX NAME)



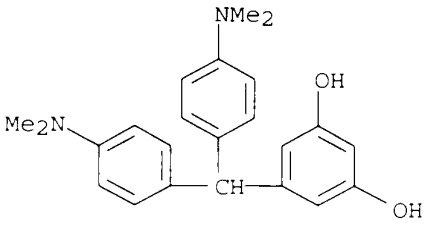
RN 77290-43-8 CAPLUS
CN Benzoic acid, 4-[bis[4-(dimethylamino)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 443893-62-7 CAPLUS
CN Phenol, 3-[bis[4-(diethylamino)phenyl]methyl]- (9CI) (CA INDEX NAME)

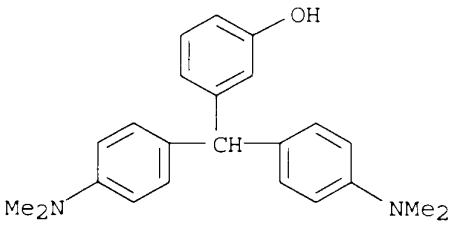


RN 443893-66-1 CAPLUS
CN 1,3-Benzenediol, 5-[bis[4-(dimethylamino)phenyl]methyl]- (9CI) (CA INDEX NAME)

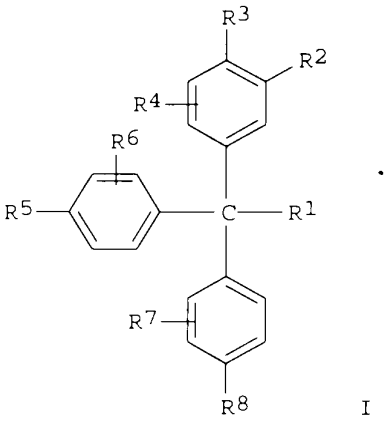


IT **116436-19-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of triphenylmethanes as kinesin KSP inhibitors)

RN 116436-19-2 CAPLUS
CN Phenol, 3-[bis[4-(dimethylamino)phenyl]methyl]- (9CI) (CA INDEX NAME)



GI



I

AB A method for treating cellular proliferative diseases comprises administration of title compds., e.g., (I; R1 = H, alkyl; R2 = H, OH, F, NH2, NO2; R3 = H, CO2H, alkoxy, OH; R4 = H, OH, alkoxycarbonyl; R5 = alkylthio, NH2, dialkylamino, OH, alkoxy, SO2Me; R6 = H, dialkylamino, OH, CO2H; R7 = H, dialkylamino, OH, CO2H; R8 = alkylthio, NH2, dialkylamino, OH, alkoxy, SO2Me). Thus, PhNMe2 and PhCHO were heated in aq. H2SO4 at 95.degree. for 48 h to give 75% bis(4-dimethylaminophenyl)phenylmethane. Several I induced mitotic arrest in Skov-3 human ovarian **cancer** cells with with Ki's <100 .mu.M.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

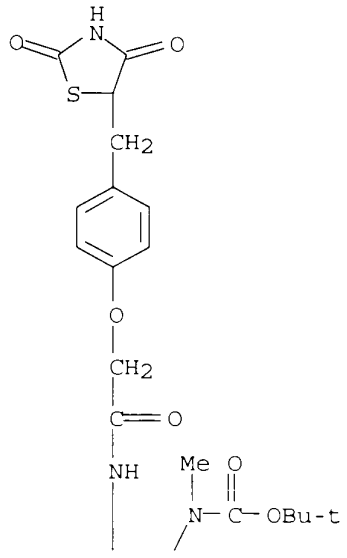
L8 ANSWER 8 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2002:479961 CAPLUS
DN 137:41755
TI Antidiabetic agents containing amine derivatives having benzimidazole or imidazopyridine ring and their other uses
IN Fujita, Takashi; Wada, Kunio; Oguchi, Minoru; Honma, Eiji; Fujiwara, Toshihiko
PA Sankyo Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 109 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

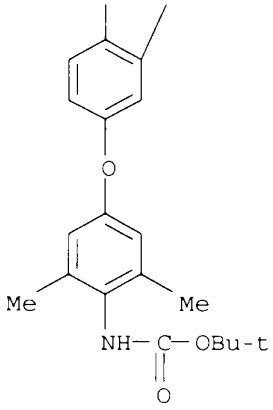
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2002179568	A2	20020626	JP 2001-308814	20011004
			JP 2000-307159 A	20001006

OS MARPAT 137:41755
IT **223132-77-2P 223133-34-4P 223134-15-4P**
223134-17-6P 301548-18-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of benzimidazole or imidazopyridine compds. as antidiabetic agents)
RN 223132-77-2 CAPLUS
CN Carbamic acid, [5-[4-[[(1,1-dimethylethoxy)carbonyl]amino]-3,5-dimethylphenoxy]-2-[[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]acetyl]amino]phenyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

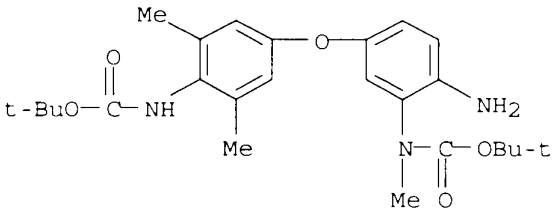
PAGE 1-A



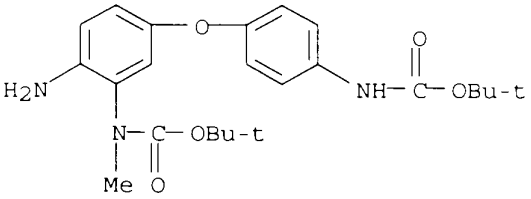
PAGE 2-A



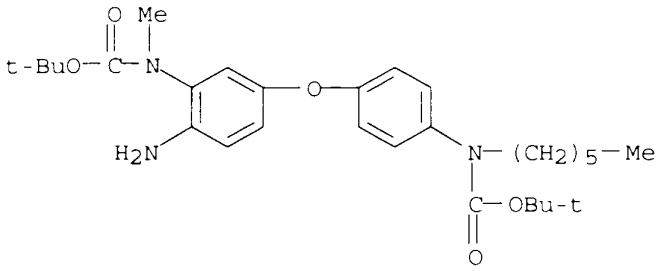
RN 223133-34-4 CAPLUS
CN Carbamic acid, [2-amino-5-[4-[[(1,1-dimethylethoxy)carbonyl]amino]-3,5-dimethylphenoxy]phenyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 223134-15-4 CAPLUS
CN Carbamic acid, [2-amino-5-[4-[[(1,1-dimethylethoxy)carbonyl]amino]phenoxy]phenyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

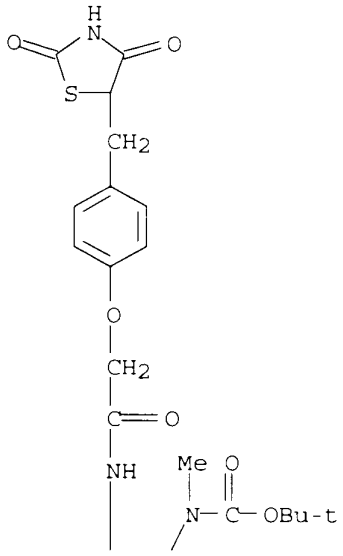


RN 223134-17-6 CAPLUS
CN Carbamic acid, [2-amino-5-[4-[[(1,1-dimethylethoxy)carbonyl]hexylamino]phenoxy]phenyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

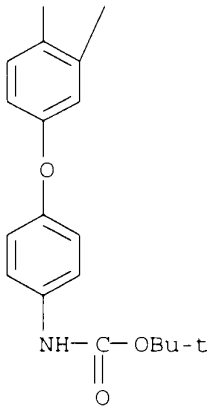


RN 301548-18-5 CAPLUS
CN Carbamic acid, [5-[4-[[(1,1-dimethylethoxy)carbonyl]amino]phenoxy]-2-[[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]acetyl]amino]phenyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

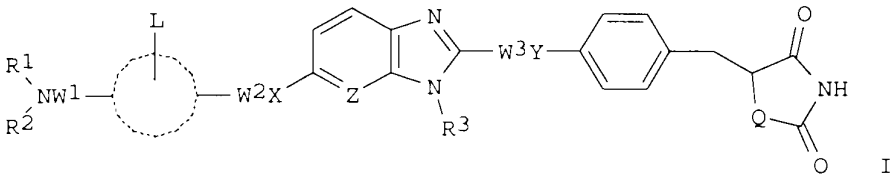
PAGE 1-A



PAGE 2-A



GI



I

AB Prophylactic and/or therapeutic agents for diabetes, glucose intolerance, diabetic complications, or gestational diabetes contain the derivs. I (R1 = carbamoyl which may have 1-2 .alpha., thiocarbamoyl which may have 1-2 .alpha., sulfonyl having 1 .alpha., carbonyl having 1 .alpha.; R2, R3 = H, C1-10 alkyl, C6-10 aryl, which may have 1-3 .beta., C7-16 aralkyl which may have 1-3 .beta. on the aryl moiety; W1-W3 = direct bond, C1-8 alkylene; X, Y, Q = O, S; Z = :CH, N' Ar = benzene or naphthalene ring substituted with 1-4 L; L = H, C1-6 alkyl, C6-10 aryl which may have 1-3 .beta., C7-16 aralkyl which may have 1-3 .beta. on the aryl moiety; definitions of .alpha. and .beta. are given) or their pharmacol. acceptable salts. I and their salts are also useful as insulin resistance improving agents, hypoglycemics, inflammation inhibitors, immunomodulators, aldose reductase inhibitors, 5-lipoxygenase inhibitors, lipid peroxide formation inhibitors, PPAR activators, antiosteoporotic agents, leukotriene antagonists, adipocyte conversion promoters, **cancer** cell growth inhibitors, and Ca blockers. Feeding diabetic KK mice with feed contg. 0.01% 1-(4-chlorophenyl)-3-[4-[2-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxymethyl]-1-methyl-1H-benzimidazol-6-yloxy]-2,6-dimethylphenyl]thiourea (II) for 3 days showed 48.9% hypoglycemic effect. Capsules, tablets, and granules contg. II were also formulated.

L8 ANSWER 9 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2002:407968 CAPLUS
DN 138:49372
TI Synthesis and pharmacological characterization of a potent, orally active p38 kinase inhibitor

AU Dumas, Jacques; Hatoum-Mokdad, Holia; Sibley, Robert N.; Smith, Roger A.; Scott, William J.; Khire, Uday; Lee, Wendy; Wood, Jill; Wolanin, Donald; Cooley, Jeffrey; Bankston, Donald; Redman, Aniko M.; Schoenleber, Robert; Caringal, Yolanda; Gunn, David; Romero, Romulo; Osterhout, Martin; Paulsen, Holger; Housley, Timothy J.; Wilhelm, Scott M.; Pirro, John; Chien, Du-Shieng; Ranges, Gerald E.; Shrikhande, Alka; Muzsi, Andrew; Bortolon, Elizabeth; Wakefield, Jean; Gianpaolo Ostravage, Cynthia; Bhargava, Ajay; Chau, Thuy

CS Department of Chemistry Research, Bayer Research Center, West Haven, CT, 06516, USA

SO Bioorganic & Medicinal Chemistry Letters (2002), 12(12), 1559-1562
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Science Ltd.

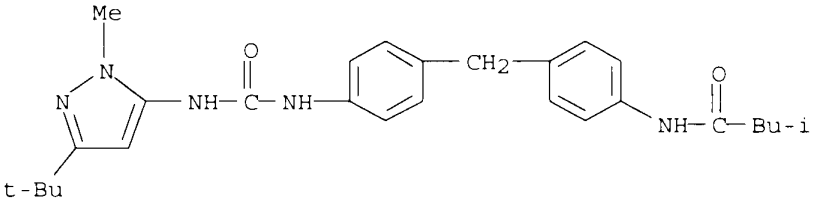
DT Journal

LA English

IT **229002-03-3 229002-04-4 229002-05-5**
229002-06-6 229002-07-7 229002-08-8
229002-09-9 229002-11-3 229002-24-8
229155-44-6 229155-45-7 229155-46-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-activity relationship, synthesis and pharmacol. characterization of a potent, orally active p38 kinase inhibitors)

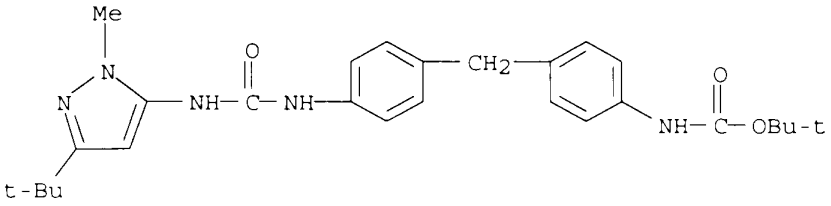
RN 229002-03-3 CAPLUS

CN Butanamide, N-[4-[[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenyl]methyl]phenyl]-3-methyl- (9CI) (CA INDEX NAME)



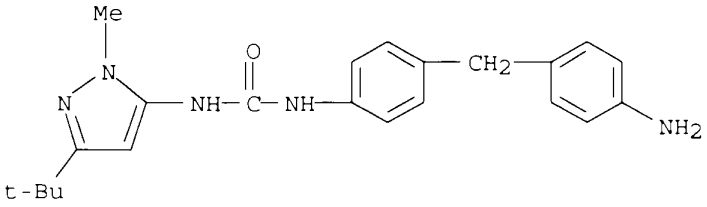
RN 229002-04-4 CAPLUS

CN Carbamic acid, [4-[[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenyl]methyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

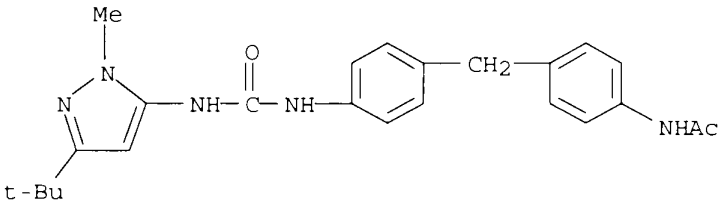


RN 229002-05-5 CAPLUS

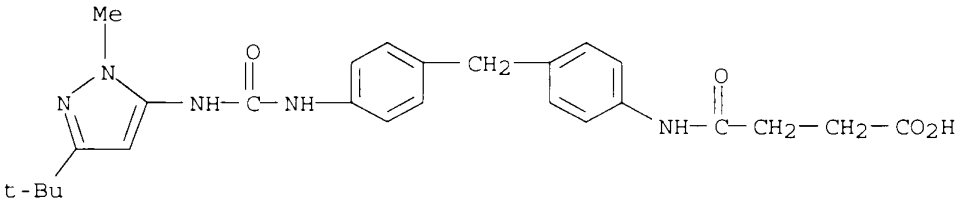
CN Urea, N-[4-[(4-aminophenyl)methyl]phenyl]-N'-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]- (9CI) (CA INDEX NAME)



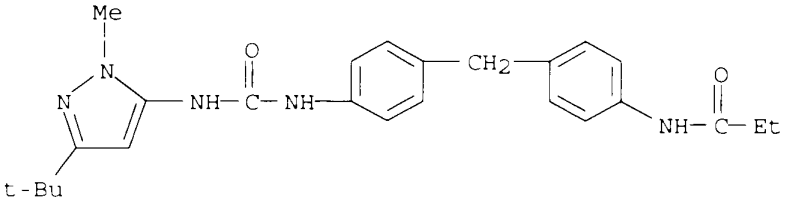
RN 229002-06-6 CAPLUS
CN Acetamide, N-[4-[[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenyl]methyl]phenyl]- (9CI) (CA INDEX NAME)



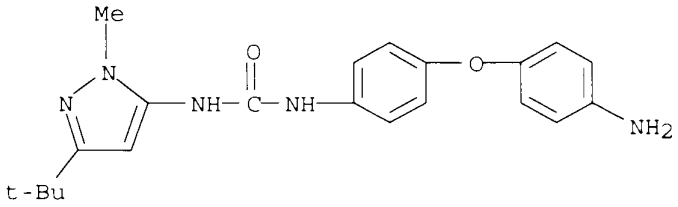
RN 229002-07-7 CAPLUS
CN Butanoic acid, 4-[[4-[[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenyl]methyl]phenyl]amino]-4-oxo- (9CI) (CA INDEX NAME)



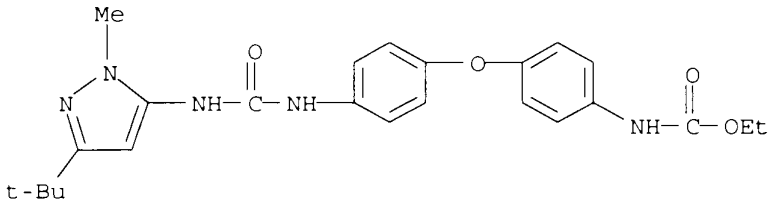
RN 229002-08-8 CAPLUS
CN Propanamide, N-[4-[[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenyl]methyl]phenyl]- (9CI) (CA INDEX NAME)



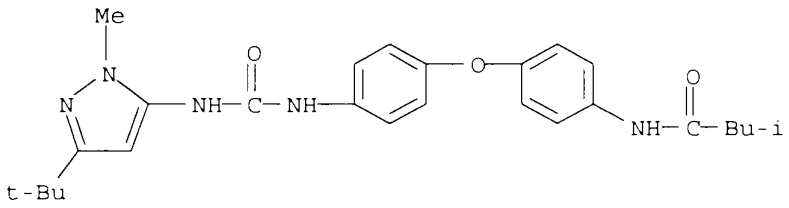
RN 229002-09-9 CAPLUS
CN Urea, N-[4-(4-aminophenoxy)phenyl]-N'-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]- (9CI) (CA INDEX NAME)



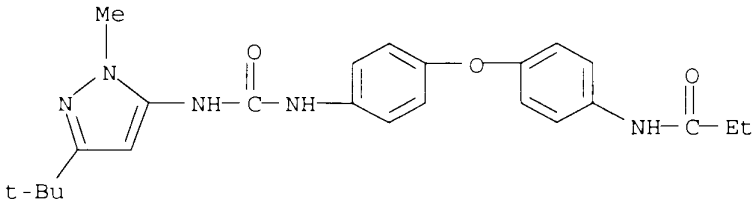
RN 229002-11-3 CAPLUS
CN Carbamic acid, [4-[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenoxy]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



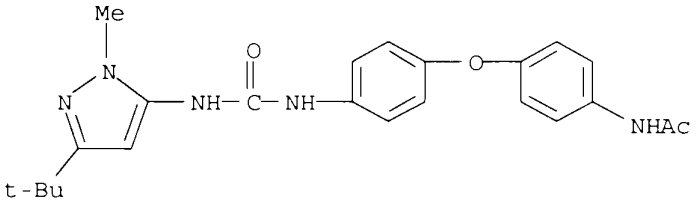
RN 229002-24-8 CAPLUS
CN Butanamide, N-[4-[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenoxy]phenyl]-3-methyl- (9CI) (CA INDEX NAME)



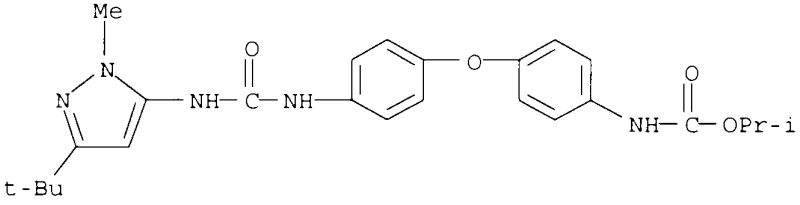
RN 229155-44-6 CAPLUS
CN Propanamide, N-[4-[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenoxy]phenyl]- (9CI) (CA INDEX NAME)



RN 229155-45-7 CAPLUS
CN Acetamide, N-[4-[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenoxy]phenyl]- (9CI) (CA INDEX NAME)



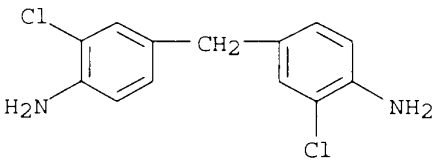
RN 229155-46-8 CAPLUS
CN Carbamic acid, [4-[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenoxy]phenyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)



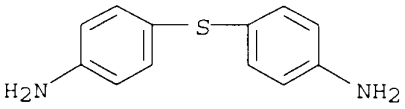
AB Inhibitors of the MAP kinase p38 provide a novel approach for the treatment of osteoporosis, inflammatory disorders, and **cancer**. We have identified N-(3-tert-butyl-1-methyl-5-pyrazolyl)-N'-(4-(4-pyridinylmethyl)phenyl)urea as a potent and selective p38 kinase inhibitor in biochem. and cellular assays. This compd. is orally active in two acute models of cytokine release (TNF-induced IL-6 and LPS-induced TNF) and a chronic model of arthritis (20-day murine collagen-induced arthritis).
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2001:919918 CAPLUS
DN 136:195524
TI Discriminant analysis of the relationship between topological molecular structure and carcinogenicity of aromatic amines
AU Kabankin, A. S.; Kurlyandskii, B. A.

CS Russian State Register of Potentially Dangerous Chemical and Biochemical Substances, Moscow, Russia
SO Pharmaceutical Chemistry Journal (Translation of Khimiko-Farmatsevticheskii Zhurnal) (2001), 35(5), 257-259
CODEN: PCJOAU; ISSN: 0091-150X
PB Kluwer Academic/Consultants Bureau
DT Journal
LA English
IT **101-14-4**, 4,4'-Methylenebis-(2-chloroaniline) **139-65-1**, 4,4'-Thiodianiline
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (discriminant anal. of relationship between topol. mol. structure and carcinogenicity of arom. amines)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



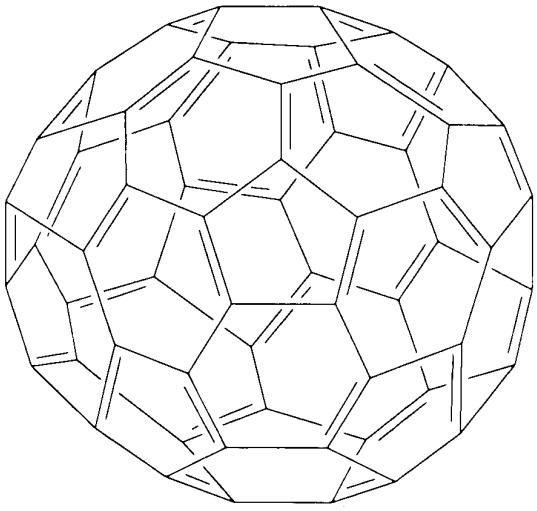
AB A linear discriminant anal. was used in predicting the ability of arom. amines to induce **cancer** in human or animals based on broad system of mol. topol. descriptors of various types. The test system consisted of 18 carcinogenic compds. for the first group and 20 noncarcinogenic arom. amines for the second group. Each mol. was characterized by almost eighty topol. descriptors, such as Wiener and Balaban indexes, metric characteristics of the mol. graphs, mol. connectivity indexes of various orders, information theory indexes, and mol. shape indexes. The most informative parameter was the ratio of the max. value of the descriptor U'(i)for carbon atoms in the benzene ring bound to the amino group. About 63% of compds. in the learning set was correctly classified when the U'max/U'min ratio was used as an independent variable. The max. predicting ability, a 78% for carcinogens and 75% for non-carcinogens, was obtained. Results showed that the topol. descriptors sufficiently substitute for the expensive quantum-chem. indexes in certain instances.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2001:866165 CAPLUS
DN 136:147154
TI DNA-cleavage by fullerene-based synzymes

AU Samal, Shashadhar; Geckeler, Kurt E.
CS Laboratory of Applied Macromolecular Chemistry, Department of Materials Science and Engineering, Kwangju Institute of Science and Technology, Kwangju, 500-712, S. Korea
SO Macromolecular Bioscience (2001), 1(8), 329-331 Published in: Macromol. Chem. Phys., 202(16)
CODEN: MBAIBU; ISSN: 1616-5187
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
IT **300829-27-0**
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(DNA-cleavage by fullerene-based synzymes: implications for use in **cancer** PDT)
RN 300829-27-0 CAPLUS
CN .beta.-Cyclodextrin, compd. with 4,4'-oxybis[benzenamine] (1:1), polymer with [5,6]fullerene-C60-Ih (9CI) (CA INDEX NAME)

CM 1

CRN 99685-96-8
CMF C60



CM 2

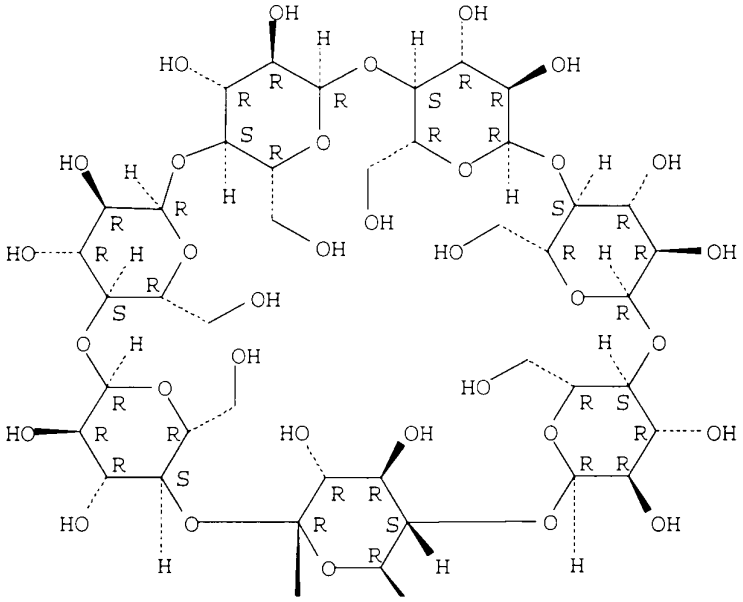
CRN 300829-25-8
CMF C42 H70 O35 . C12 H12 N2 O

CM 3

CRN 7585-39-9
CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



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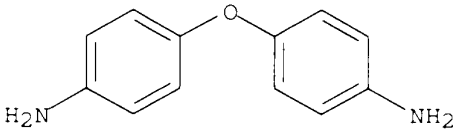
CM 4

CRN 101-80-4
CMF C12 H12 N2 O



AB Efficient cleaving of DNA oligonucleotides by a water-sol. fullerene main-chain polymer is demonstrated following a facile routine of monitoring the reaction by UV-vis spectroscopy and sepg. the cleaved fractions by membrane filtration. A small quantity of the fullerene deriv. could cleave a large excess of the oligonucleotide under ambient light conditions, leading to cleaved DNA in quant. yields.

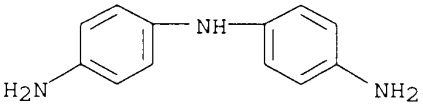
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2001:569803 CAPLUS
DN 135:177699
TI Detecting **cancer** by histochemical staining
IN Cottington, Kay
PA UK
SO Brit. UK Pat. Appl., 38 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

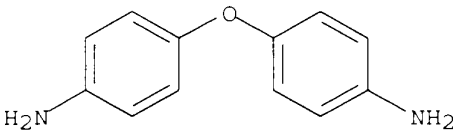
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2355790	A1	20010502	GB 1999-25314	19991027
			GB 1999-25314	19991027

IT **537-65-5**, p-p'-Diaminodiphenylamine
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(derivs.; detecting **cancer** by histochem. staining)
RN 537-65-5 CAPLUS
CN 1,4-Benzenediamine, N-(4-aminophenyl)- (9CI) (CA INDEX NAME)

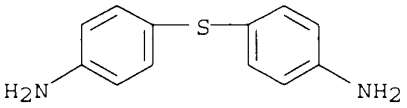


AB Presence of **cancer** or precancerous cells in samples of biol. material is detected by color screening. Typically, enzyme activity in the material is detected histochem., e.g., using a dye or stain, to indicate the presence of a **cancer** in a tissue sample. ATPase activity was detected in frozen tissue sections using sodium ATP, calcium chloride, sodium phosphate, CoCl2, and yellow ammonium sulfide.

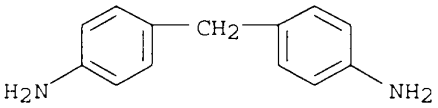
L8 ANSWER 13 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2001:503223 CAPLUS
DN 135:252853
TI A simple method for quantitative risk assessment of non-threshold carcinogens based on the dose descriptor T25
AU Sanner, Tore; Dybing, Erik; Willems, Marianne I.; Kroese, E. Dinant
CS Department of Environmental and Occupational Cancer, Institute for Cancer Research, The Norwegian Radium Hospital, Oslo, N-0310, Norway
SO Pharmacology & Toxicology (Copenhagen, Denmark) (2001), 88(6), 331-341
CODEN: PHTOEH; ISSN: 0901-9928
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
IT **101-80-4**, 4,4'-Oxydianiline **139-65-1**, 4,4'-Thiodianiline **13552-44-8**, 4,4'-Methylenedianiline dihydrochloride
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(method for quant. risk assessment of non-threshold carcinogens based on dose descriptor T25)
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



RN 13552-44-8 CAPLUS
CN Benzenamine, 4,4'-methylenebis-, dihydrochloride (9CI) (CA INDEX NAME)

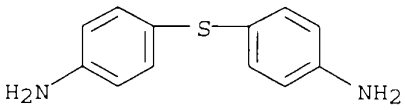


●2 HCl

AB This report provides guidance for using the dose-descriptor T25 from animal studies as a basis for quant. risk characterization of non-threshold carcinogens. T25 is presently used within the European Union for setting specific concn. limits for carcinogens in relation to labeling of prepns. (formulations). The T25 is defined as the chronic dose rate which will give 25% of the animals tumors at a specific tissue site, after correction for spontaneous incidence, within the std. life-time of that species. The T25 is converted to the corresponding human dose descriptor, HT25, by dividing it with the appropriate scaling factor for interspecies dose scaling based on comparative metabolic rates. Subsequently, the human dose (expressed in mg per kg body-wt. per day) is calcd. from the available exposure data. The corresponding human life-time **cancer** risk is then obtained by using linear extrapolation by dividing the exposure dose with the coeff. (HT25/0.25). The results with this new method, which can easily be calcd. without computer programs, are in excellent agreement with results from computer-based extrapolation methods such as the linearised multistage model and the benchmark method using LED10, even though the present method only takes into consideration one single dose-response point. To overcome possible shortcomings of the present method, the estd. life-time risks are proposed to be accompanied by a commentary statement giving an overall evaluation of data that may have bearing on the carcinogenic risk and that may indicate whether the real human risk is likely to be higher or lower than the calcd. life-time risk. By using the present guidance and a harmonized set of criteria and default values, the calcn. of life-time

cancer risk should be transparent and easy to comprehend.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2001:475934 CAPLUS
DN 135:253067
TI Data quality in predictive toxicology: Reproducibility of rodent carcinogenicity experiments
AU Gottmann, Eva; Kramer, Stefan; Pfahringer, Bernhard; Helma, Christoph
CS Institute for Cancer Research, University Vienna, Vienna, Austria
SO Environmental Health Perspectives (2001), 109(5), 509-514
CODEN: EVHPAZ; ISSN: 0091-6765
PB National Institute of Environmental Health Sciences
DT Journal
LA English
IT **139-65-1**, 4,4'-Thiodianiline
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(data quality in predictive toxicol. and reproducibility of rodent carcinogenicity expts.)
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



AB We compared 121 replicate rodent carcinogenicity assays from the two parts (National **Cancer** Institute/National Toxicol. Program and literature) of the Carcinogenic Potency Database (CPDB) to est. the reliability of these expts. We estd. a concordance of 57% between the overall rodent carcinogenicity classifications from both sources. This value did not improve substantially when addnl. biol. information (species, sex, strain, target organs) was considered. These results indicate that rodent carcinogenicity assays are much less reproducible than previously expected, an effect that should be considered in the development of structure-activity relationship models and the risk assessment process.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2001:338762 CAPLUS
DN 134:362292
TI Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
IN Farr, Spencer
PA Phase-1 Molecular Toxicology, USA
SO PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

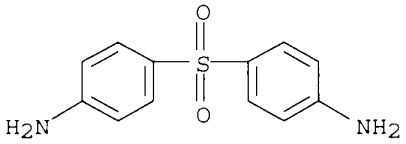
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2001032928 A2 20010510 WO 2000-US30474 20001103
WO 2001032928 A3 20020725
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 1999-165398PP 19991105
US 2000-196571PP 20000411

IT **80-08-0**, Dapsone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

RN 80-08-0 CAPLUS

CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L8 ANSWER 16 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2001:185778 CAPLUS
DN 134:237837
TI Preparation of dolastatin peptides
IN Petit, George R.; Srirangam, Jayaram K.; Williams, Michael D.; Durkin, Kieran P. M.; Barlozzari, Teresa; Kling, Andreas; Janssen, Bernd; Haupt, Andreas
PA Basf Aktiengesellschaft, Germany; Arizona Board of Regents

SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001018032	A2	20010315	WO 2000-US24658	20000908
	WO 2001018032	A3	20020711		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

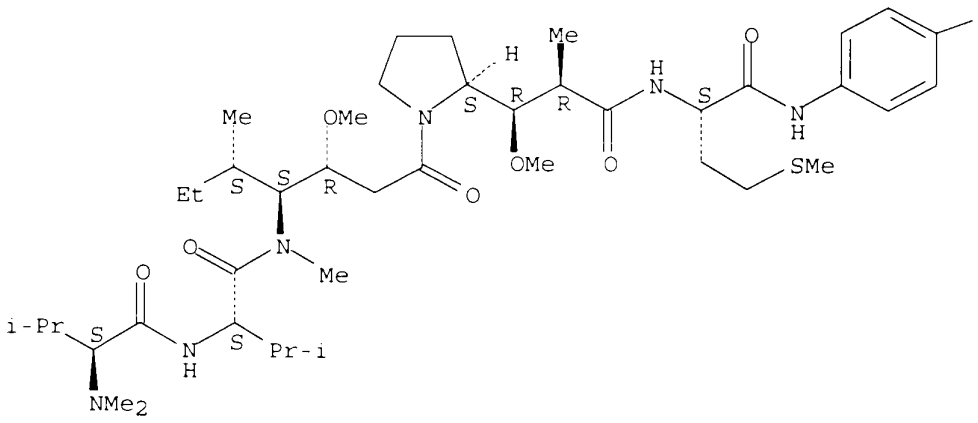
US 1999-394962 A119990910
US 2000-539935 A120000331

	US 6323315	B1	20011127	US 2000-539935	20000331
				US 1999-394962 B119990910	

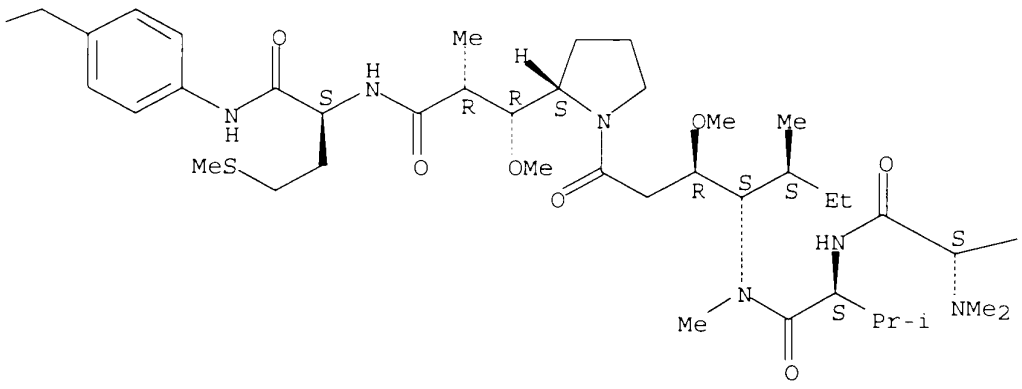
OS MARPAT 134:237837
IT **329792-13-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of dolastatin peptides)
RN 329792-13-4 CAPLUS
CN L-Methioninamide, 5,5'-(methylenedi-4,1-phenylene)bis[N,N-dimethyl-L-valyl-L-valyl-(3R,4S,5S)-3-methoxy-5-methyl-4-(methylamino)heptanoyl-(.alpha.R,.beta.R,2S)-.beta.-methoxy-.alpha.-methyl-2-pyrrolidinepropanoyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



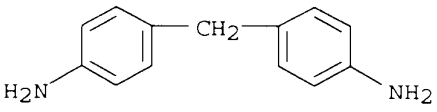
PAGE 1-B



PAGE 1-C

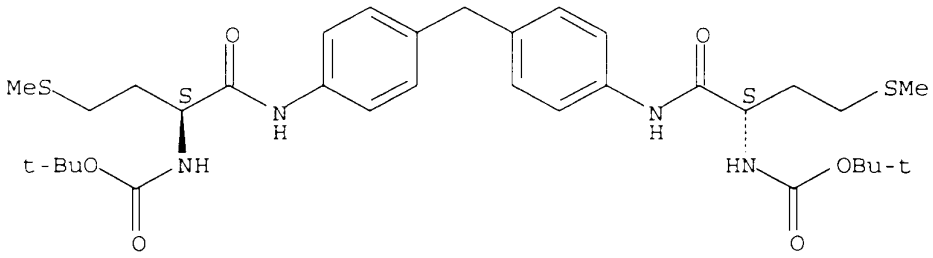
—Pr-i

IT **101-77-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of dolastatin peptides)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



IT **329791-90-4P 329791-97-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of dolastatin peptides)
RN 329791-90-4 CAPLUS
CN Carbamic acid, [methylenebis[4,1-phenyleneimino[(1S)-1-[2-(methylthio)ethyl]-2-oxo-2,1-ethanediyl]]]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

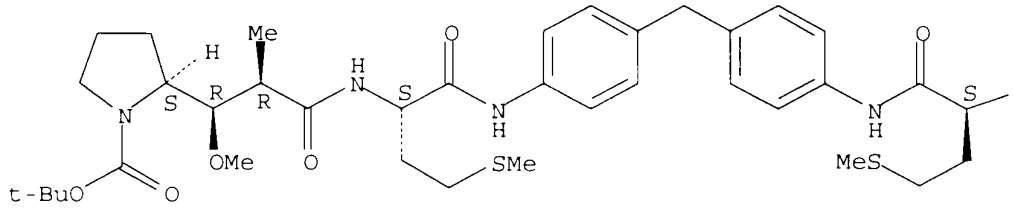
Absolute stereochemistry. Rotation (-).



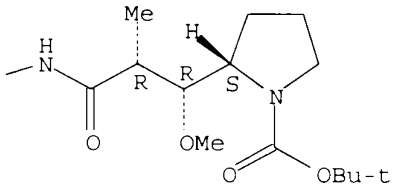
RN 329791-97-1 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, [methylenebis[4,1-phenyleneimino[(1S)-1-[2-(methylthio)ethyl]-2-oxo-2,1-ethanediyl]imino[(1R,2R)-1-methoxy-2-methyl-3-oxo-3,1-propanediyl]]]bis-, bis(1,1-dimethylethyl) ester, (2S,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

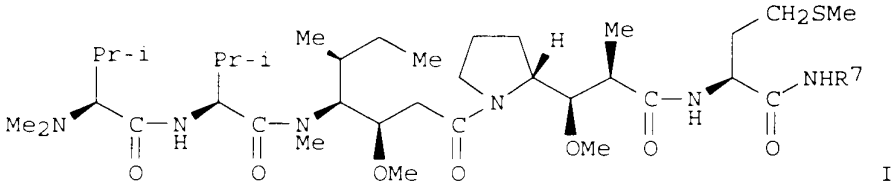
PAGE 1-A



PAGE 1-B



GI



I

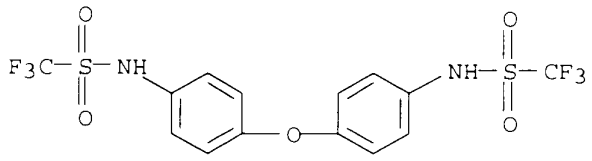
AB Peptides R1R2NCHR3CONHCHR4CONMeCHR5CH(OMe)CH2CONRCHRCH(OMe)CHMeCO-An-NR6R7 [R2 = (CH2)3; R1-R5 are each independently H or C1-C6 alkyl; A is a methionyl, phenylalanyl or phenylglycyl residue; n is 0 or 1; R6 is H and R7 is a carbocyclic, arom., alkyl, pyridylalkyl, or heterocyclic group or R6 is benzyl or carbalkoxy and R7 is 2-thiazolyl] or their pharmaceutically acceptable salts were prepd. for use as cell growth inhibitors. Thus, I [R7 = bicyclo[3.3.0]octan-1-yl] was prepd. by soln. phase methods and evaluated for in vitro cytotoxicity against a panel of cultured **cancer** cell lines, including OVCAR-3 (ovarian **cancer**), ED50 = 3.1 x 10-4 .mu.g/mL.

L8 ANSWER 17 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2001:167962 CAPLUS
DN 134:222529
TI Preparation of aromatic trifluoromethylsulfonyl and trifluoromethylsulfonamido compounds as phosphate mimics and phosphatase inhibitors and methods of treatment
IN Huang, Ping; Wei, Chung Chen; Tang, Peng Cho; Liang, Chris; Ramphal, John; Jallal, Bahija; Blitz, John; Li, Sharon; Mattson, Matthew Neil; Mcahon, Gerald; Koenig, Marcel
PA Sugen, Inc., USA; et al.
SO PCT Int. Appl., 262 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

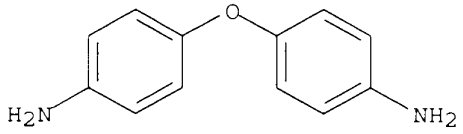
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001016097	A1	20010308	WO 2000-US23293	20000825
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
				US 1999-150970PP	19990827
				US 1999-165365PP	19991112
	EP 1212296	A1	20020612	EP 2000-961360	20000825
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
				US 1999-150970PP	19990827
				US 1999-165365PP	19991112
				WO 2000-US23293W	20000825
	JP 2003508382	T2	20030304	JP 2001-519667	20000825
				US 1999-150970PP	19990827
				US 1999-165365PP	19991112
				WO 2000-US23293W	20000825

OS MARPAT 134:222529
IT **32359-97-0P**, Bis(4-trifluoromethylsulfonamidophenyl) ether
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of arom. trifluoromethylsulfonyl and trifluoromethylsulfonamido compds. as phosphate mimics and phosphatase inhibitors)

RN 32359-97-0 CAPLUS
CN Methanesulfonamide, N,N'-(oxydi-4,1-phenylene)bis[1,1,1-trifluoro- (9CI) (CA INDEX NAME)



IT **101-80-4**, 4,4'-Diaminodiphenyl ether
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; prepn. of arom. trifluoromethylsulfonyl and trifluoromethylsulfonamido compds. as phosphate mimics and phosphatase inhibitors)
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to trifluoromethyl sulfonyl and trifluoromethyl sulfonamido compds. and their physiol. acceptable salts and prodrugs. In particular, compds. I, II, and III are claimed [wherein: Q = CF3SO2, CF3SO2NR3, CF3SO2R4, or CF3SO2N(R3)R4; R1 = H, alkyl, haloalkyl, cyano, CO2H or derivs., halo, OH or derivs., NH2 or derivs., etc.; R2 = H, groups similar to R1; R3 = H, (un)substituted alkoxy, acyl, or alkyl; R4 = (un)substituted CH2; n = 0-3; B = atoms to complete (un)substituted fused aryl, carbocyclyl, heteroaryl, or heterocyclyl ring; A1 = (un)substituted and/or heteroatom-replaced linkage of 2-8 atoms length; A2 = similar linkage of 0-6 atoms]. These compds. are expected to modulate the activity of protein tyrosine enzymes which are related to cellular signal transduction, in particular, protein tyrosine phosphatase (PTP), and therefore are expected to be useful in the prevention and treatment of disorders assocd. with abnormal protein tyrosine enzyme related cellular signal transduction such as **cancer**, diabetes, immuno-modulation, neurol. degenerative diseases, osteoporosis and infectious diseases. The invention also relates to the use of compds. contg. fluoromethyl sulfonyl groups as phosphate mimics. These mimics may be used to inhibit, regulate or modulate the activity of a phosphate binding protein in a cell. Over 100 compds. were prepd., and most were assayed against selected PTPs. For example, etherification of Me 4-(2-hydroxyethoxy)benzoic acid Me ester with 2-nitro-4-(trifluoromethylsulfonyl)chlorobenzene using NaH, and

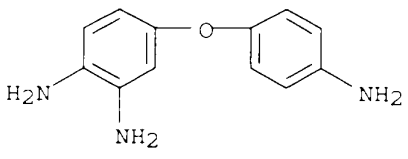
hydrolysis with HCl in aq. THF-EtOH, gave title compd. IV. This compd. had IC50 values as follows (.mu.M): PTP 1B = 1.5, PTP MEG2 = 1.5, PTP .alpha. = 22.2.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2001:12273 CAPLUS
DN 134:86271
TI Preparation of pyrimidine derivatives as Src-family protein tyrosine kinase inhibitor compounds
IN Armstrong, Helen M.; Beresis, Richard; Goulet, Joung L.; Holmes, Mark A.; Hong, Xingfang; Mills, Sander G.; Parsons, William H.; Sinclair, Peter J.; Steiner, Mark G.; Wong, Frederick; Zaller, Dennis M.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 470 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001000213	A1	20010104	WO 2000-US17443	20000626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
			US 1999-141639PP	19990630
EP 1206265	A1	20020522	EP 2000-941701	20000626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
			US 1999-141639PP	19990630
			WO 2000-US17443W	20000626
US 6498165	B1	20021224	US 2000-604305	20000626
			US 1999-141639PP	19990630

OS MARPAT 134:86271
IT **6264-66-0**, 3,4,4'-Triaminodiphenyl ether
RL: RCT (Reactant); RACT (Reactant or reagent)
(for prepn. of pyrimidine derivs. as Src-family protein tyrosine kinase inhibitor compds.)
RN 6264-66-0 CAPLUS
CN 1,2-Benzenediamine, 4-(4-aminophenoxy)- (9CI) (CA INDEX NAME)



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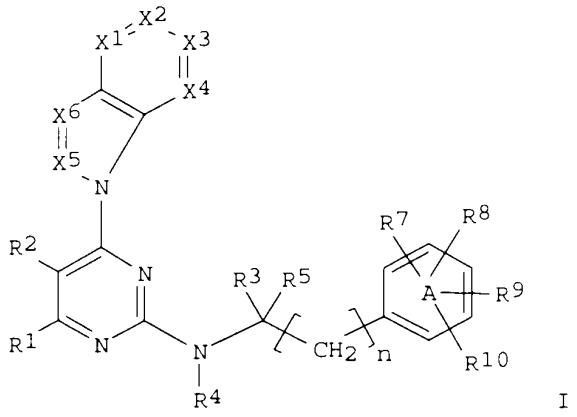


I

AB What are claimed are pyrimidine compds. (shown as I), or their pharmaceutically acceptable salts, hydrates, solvates, crystal forms and individual diastereomers, and pharmaceutical compns. including the same and their use as inhibitors of tyrosine kinase enzymes and consequently their use in the prophylaxis and treatment of protein tyrosine kinase-assocd. disorders, such as immune diseases, hyperproliferative disorders and other diseases in which inappropriate protein kinase action is believed to play a role, such as **cancer**, angiogenesis, atherosclerosis, graft rejection, rheumatoid arthritis and psoriasis. In I, R1, R2 = independently H, halo, OH, SH, CN, NO2, alkyl, alkoxy, acyloxy, alkoxycarbonyloxy, carbamoyloxy, alkylthio, sulfinyl, sulfonyl, acyl, alkoxycarbonyl, carbamoyl, amino, acylamino, ureido, sulfamoyl, sulfonylamino, or R1 and R2 can join together to form a fused methylenedioxy ring or a fused 6-membered arom. ring; terms such as 'alkyl' here and below are further defined in the claims. R3, R5 = independently H, C1-C6-alkyl unsubstituted or substituted with 1-3 substituents, aryl, or R3 and R5 taken together can represent :O; R3 or R5 can represent a 2 or 3 C methylene bridge forming a ring of 5-8 atoms fused to the A ring. R4 = H, C1-C6-alkyl, C1-C6-alkoxyl. X1, X2, X3, X4 in -X1:X2-X3:X4- are substituted or unsubstituted CH or N where 0-2 of X1, X2, X3, X4 are N. X5, X6 = independently N, C, optionally substituted CH. A ring = Ph, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, furanyl, benzothienyl, benzofuranyl, indolyl, imidazolyl, benzimidazolyl, thiadiazolyl. R7, R8, R9, R10 = independently H, halo, OH, SH, CN, NO2, N3, N2+BF4-, alkyl, alkoxy, alkylthio, sulfinyl, sulfonyl, C1-C6-alkyl, C1-C6-perfluoroalkyl, acyl, alkoxycarbonyl, carbamoyl, acyloxy, alkoxycarbonyloxy, carbamoyloxy, amino, acylamino, ureido, sulfamoyl, sulfonylamino, two of R7, R8, R9, and R10 when on adjacent carbons join together to form a methylenedioxy bridge. N = 0-2. More than 500 example prepns. are given, but no preparative method is claimed and no data relating to the usefulness of the compds. are given.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

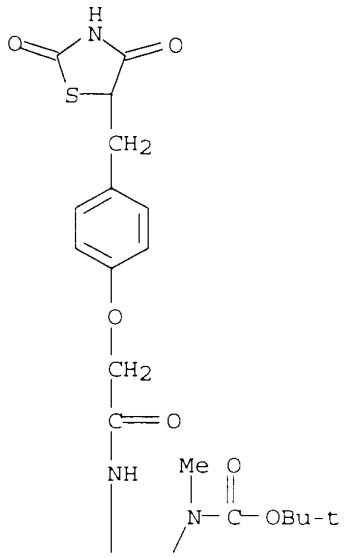
L8 ANSWER 19 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2000:742094 CAPLUS

DN 133:296435
TI Preparation of amine derivatives useful agents for diabetes, hyperlipemia, arteriosclerosis, and **cancer**
IN Fujita, Takashi; Wada, Kunio; Oguchi, Minoru; Honma, Hidehito; Fujiwara, Toshihiko
PA Sankyo Company, Limited, Japan
SO PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000061581	A1	20001019	WO 2000-JP2216	20000406
W: AU, BR, CA, CN, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PL, RU, TR, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
			JP 1999-99981	A 19990407
JP 2000351779	A2	20001219	JP 2000-104702	20000406
			JP 1999-99981	A 19990407
EP 1167366	A1	20020102	EP 2000-915362	20000406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
			JP 1999-99981	A 19990407
			WO 2000-JP2216	W 20000406
BR 2000009594	A	20020604	BR 2000-9594	20000406
			JP 1999-99981	A 19990407
			WO 2000-JP2216	W 20000406
NO 2001004847	A	20011207	NO 2001-4847	20011005
			JP 1999-99981	A 19990407
			WO 2000-JP2216	W 20000406
US 2003078426	A1	20030424	US 2001-971634	20011005
			JP 1999-99981	A 19990407
			WO 2000-JP2216	A220000406

OS MARPAT 133:296435
IT **223132-77-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of amine derivs. as useful agents for diabetes, hyperlipemia, arteriosclerosis, and **cancer**)
RN 223132-77-2 CAPLUS
CN Carbamic acid, [5-[4-[[(1,1-dimethylethoxy)carbonyl]amino]-3,5-dimethylphenoxy]-2-[[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]acetyl]amino]phenyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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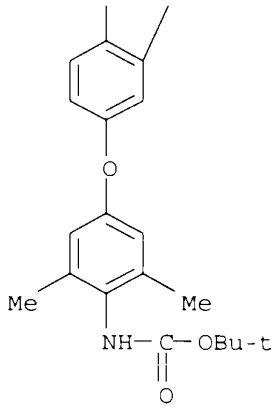
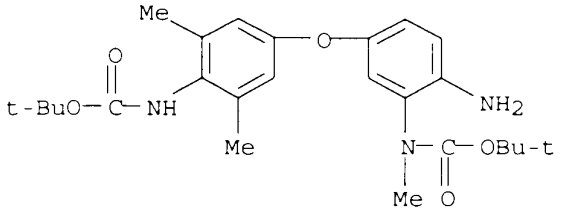


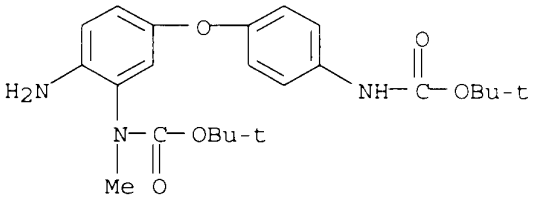
IT **223133-34-4P 223134-15-4P 223134-17-6P 301548-17-4P 301548-18-5P 301548-35-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amine derivs. as useful agents for diabetes, hyperlipemia, arteriosclerosis, and **cancer**)

RN 223133-34-4 CAPLUS

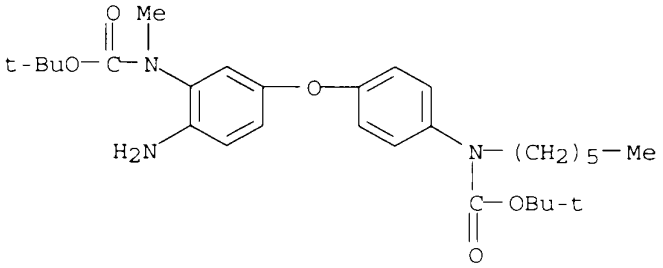
CN Carbamic acid, [2-amino-5-[4-[[(1,1-dimethylethoxy)carbonyl]amino]-3,5-dimethylphenoxy]phenyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 223134-15-4 CAPLUS
CN Carbamic acid, [2-amino-5-[4-[[(1,1-dimethylethoxy)carbonyl]amino]phenoxy]phenyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

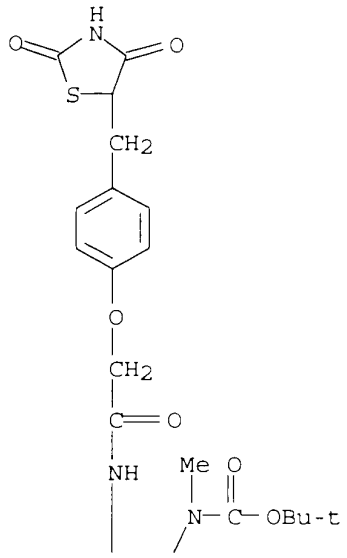


RN 223134-17-6 CAPLUS
CN Carbamic acid, [2-amino-5-[4-[[(1,1-dimethylethoxy)carbonyl]hexylamino]phenoxy]phenyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 301548-17-4 CAPLUS
CN Carbamic acid, [5-[4-[(butoxycarbonyl)amino]-3,5-dimethylphenoxy]-2-[[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]acetyl]amino]phenyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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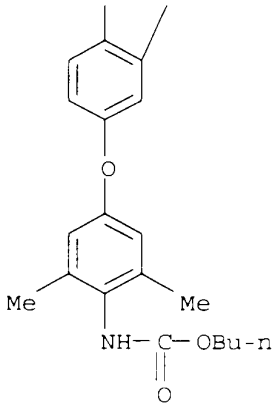
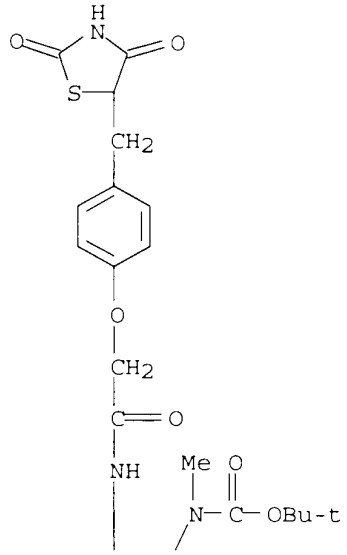


RN 301548-18-5 CAPLUS
CN Carbamic acid, [5-[4-[[(1,1-dimethylethoxy)carbonyl]amino]phenoxy]-2-[[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]acetyl]amino]phenyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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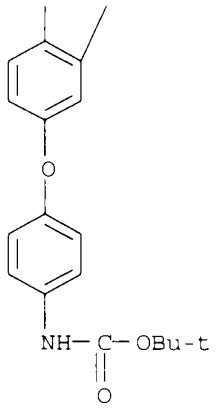
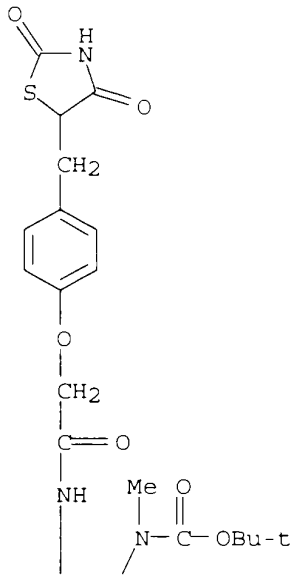


RN 301548-35-6 CAPLUS
CN Carbamic acid, [2-[[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]acetyl]amino]-5-[4-[[(1-naphthalenylamino)carbonyl]amino]phenoxy]phenyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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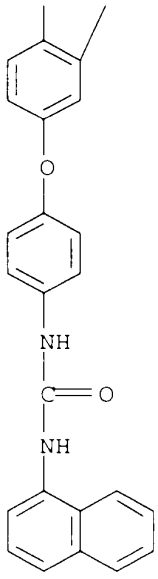


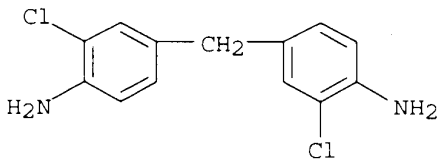
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

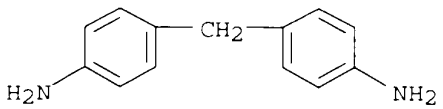
AB Title compds. [I; X = O, S; A = 1,4-C6H4, 1,3-C6H4, 1,7-naphthyl; L = H, 2,6-(CH3)2, 2-(CH3)3C, 6-(CH3)3C; R1 = CH3NHCO, CH3CH2NHCO, (CH3)3CNHCO, CH3(CH2)5NHCO, CF3NHCO, C6H5NHCO, 2-CH3C6H4NHCO, 3-CH3C6H4NHCO, 4-CH3C6H4NHCO, 2,6-(CH3)2C6H3NHCO, 4-CF3C6H4NHCO, 2,3-F2C6H4NHCO; q = 0-8; m = 0-8; n = 0-8] and pharmacol. acceptable salts, which are useful as therapeutic and/or preventive agents for diabetes, hyperlipemia, arteriosclerosis, **cancers**, are prepd. Thus, the title compd. II was prepd.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

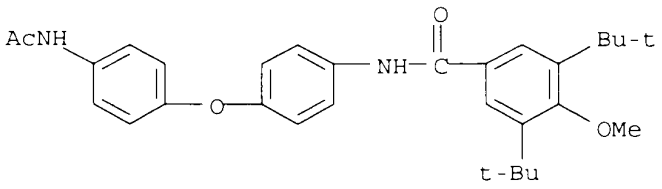
L8 ANSWER 20 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2000:230755 CAPLUS
Correction of: 1997:93197
DN 132:218255
Correction of: 126:153876
TI Evaluation of the rodent micronucleus assay in the screening of IARC carcinogens (Groups 1, 2A and 2B). The summary report of the 6th collaborative study by CSGMT/JEMS.cntdot.MMS
AU Morita, Takeshi; Asano, Norihide; Awogi, Takumi; Sasaki, Yu F.; Sato, Sei-ichi; Shimada, Hiroyasu; Sutou, Sizuyo; Suzuki, Takayoshi; Wakata, Akihiro; Sofuni, Toshio; Hayashi, Makoto
CS Nippon Glaxo Ltd., Ibaraki, 300-42, Japan
SO Mutation Research (1997), 389(1), 3-122
CODEN: MUREAV; ISSN: 0027-5107
PB Elsevier
DT Journal
LA English
IT **101-14-4 101-77-9**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogens genotoxicity as detd. by micronucleus assay)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



AB To assess the correlation between micronucleus induction and human carcinogenicity, the rodent micronucleus assay was performed on known and



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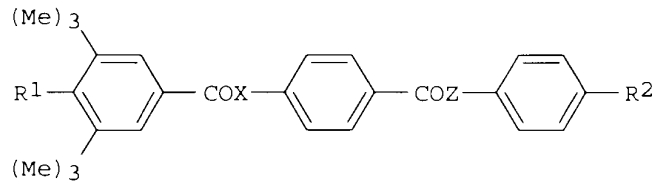


I

AB The chalone derivs. (I), R1-(3,5-di-t-butyl-1,4-phenylene)-CO-X-(1,4-phenylene)-CO-Z-(1,4-phenylene)-R4 (R1 = OH, or C1-5 alkoxy; R2 = OH, COOH, C1-5 carboxylalkyl, or NHCOR3; R3 = C1-4 alkyl; X = NH, or C2-4 alkenyl; and Z = NH, or O), are prepd. by dissolving chalone deriv. in anhyd. org. solvent, adding substituted amine and alkyl-haloformate (ester) in dropwise, stirring for 0.2-3.0 h, adding petroleum ether, filtering, concg. in vacuum, dissolving in anhyd. org. solvent, adding alkylphenol, heating to be clear, adding substituted amine and DMAP, stirring at 40-60.degree. for 0.5-3 h, concg., crystg., filtering, washing, and recrystg. with 90-99% ethanol. The medicinal compn. is composed of the chalone deriv., and medicinal carrier. The medicinal compn. may contain more than one anti-tumor drug and a immunoregulator. The medicinal compn. is used for treatment of **cancer**.

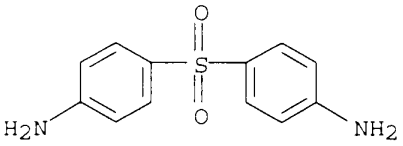
L8 ANSWER 22 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2000:112755 CAPLUS
DN 132:176869
TI Chemical carcinogenicity: can it be predicted from knowledge of mutagenicity and allergic contact dermatitis?
AU Rosenkranz, Herbert S.; Karol, Meryl H.
CS Department of Environmental and Occupational Health, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA, 15261, USA
SO Mutation Research (1999), 431(1), 81-91
CODEN: MUREAV; ISSN: 0027-5107
PB Elsevier Science B.V.
DT Journal
LA English
IT **80-08-0 101-77-9 101-80-4 139-65-1 1807-55-2**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(chem. carcinogenicity and prediction from knowledge of mutagenicity and allergic contact dermatitis)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)

potential human carcinogens in the 6th MMS/CSGMT collaborative study. Approx. 100 com. available chems. and chem. groups on which there was little or no micronucleus assay data were selected from IARC (International Agency for Research on **Cancer**) Groups 1 (human carcinogen), 2A (probable human carcinogen) and 2B (possible human carcinogen). As min. requirements for the collaborative study, 5 male mice were treated by i.p. injection or oral gavage once or twice with each chem. at three dose levels, and bone marrow and/or peripheral blood was analyzed. Five positives and 2 inconclusives out of 13 Group 1 chems., 7 positives and 5 inconclusives of 23 Group 2A chems., and 26 positives and 6 inconclusives of 67 Group 2B chems. were found. Such low pos. rates were not surprising because of a test chem. selection bias, and we excluded well-known micronucleus inducers. The overall evaluation of the rodent micronucleus assay was based on the present data combined with published data on the IARC carcinogens. After merging, the pos. rates for Groups 1, 2A and 2B were 68.6, 54.5 and 45.6%, resp. Structure-activity relation anal. suggested that the micronucleus assay is more sensitive to the genetic toxicity of some classes of chems. Those to which it is sensitive consist of (1) aziridines and bis(2-chloroethyl) compds.; (2) alkyl sulfonate and sulfates; (3) acyl-type N-nitroso compds.; (4) hydrazines; (5) aminobiphenyl and benzidine derivs.; and (6) azo compds. Those to which it is less sensitive consist of (1) dialkyl type N-nitroso compds.; (2) silica and metals and their compds.; (3) arom. amines without other functional groups; (4) halogenated compds.; and (5) steroids and other hormones. After incorporation of structure-activity relation information, the pos. rates of the rodent micronucleus assay became 90.5, 65.2 and 60.0% for IARC Groups 1, 2A and 2B, resp. Noteworthy was the tendency of the test to be more sensitive to those carcinogens with stronger evidence human carcinogenicity.

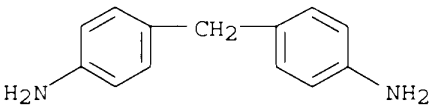
L8 ANSWER 21 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2000:151752 CAPLUS
DN 132:161237
TI Chalone retinoids as antitumor agents
IN Han, Rui; Guo, Zongru
PA Institute of Materia Medica, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 19 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1187185	A	19980708	CN 1996-194473	19960607
				CN 1996-194473	19960607

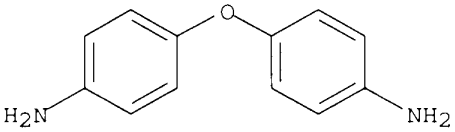
OS MARPAT 132:161237
IT **258834-44-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(chalone retinoids as antitumor agents)
RN 258834-44-5 CAPLUS
CN Benzamide, N-[4-[4-(acetylamino)phenoxy]phenyl]-3,5-bis(1,1-dimethylethyl)-4-methoxy- (9CI) (CA INDEX NAME)



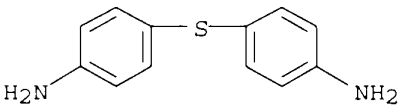
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



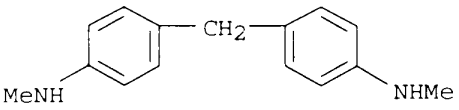
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



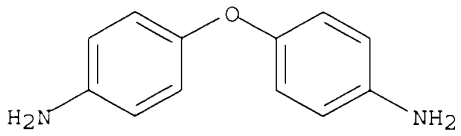
RN 1807-55-2 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N-methyl- (9CI) (CA INDEX NAME)



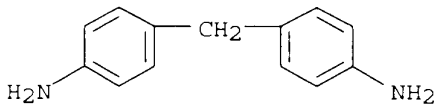
AB We investigated the suggestion [R.E. Albert, (1997)] that results of mutagenicity testing in Salmonella combined with allergic contact dermatitis (ACD) testing in humans would be predictive of carcinogenicity in rodents. Using the **cancer** bioassay results of the US National Toxicol. Program (NTP), Salmonella mutagenicity tests and a highly predictive structure-activity relational model of ACD, we conclude that the combination is not more predictive than the results of the Salmonella mutagenicity assay alone.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2000:51735 CAPLUS
DN 132:218070
TI Prediction of rodent carcinogenicity utilizing a battery of in vitro and in vivo genotoxicity tests
AU Kim, Byung Soo; Margolin, Barry H.
CS Department of Applied Statistics, Yonsei University, Seoul, 120-749, S. Korea
SO Environmental and Molecular Mutagenesis (1999), 34(4), 297-304
CODEN: EMMUEG; ISSN: 0893-6692
PB Wiley-Liss, Inc.
DT Journal
LA English
IT **101-80-4**, 4,4'-Oxydianiline **13552-44-8**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogen carcinogenicity in rodent prediction by utilizing a battery of in vitro and in vivo genotoxicity tests)
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



RN 13552-44-8 CAPLUS
CN Benzenamine, 4,4'-methylenebis-, dihydrochloride (9CI) (CA INDEX NAME)

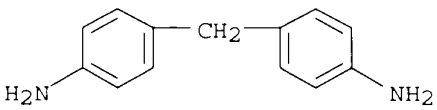


●2 HCl

AB The primary purpose of this study is to investigate the degree to which we the prediction of rodent carcinogenicity (CA) can be improved by combining results from an in vitro and two in vivo genotoxicity tests. The authors used the Ames Salmonella assay (SAL) for the in vitro test and the micronucleus assay (MNC) and chromosome aberration assay (ABS) in mouse bone marrow cells for the two in vivo tests. The authors collected complete assay data for 82 chems. (55 carcinogens and 27 noncarcinogens) from the NTP data base and the IARC monograph series. These results indicate that: (1) only SAL affects the predictivity of CA, (2) MNC has a strong assocn. with ABS, and (3) SAL predicts ABS. It has been known for some time that once the SAL assay result is available for prediction, other in vitro mutation tests provide little addnl. information for predicting CA. This study indicates that the same conclusion holds for CA, SAL, MNC, and ABS.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 2000:51727 CAPLUS
DN 132:247233
TI Carcinogenic chemical-response "fingerprint" for male F344 rats exposed to a series of 195 chemicals: implications for predicting carcinogens with transgenic models
AU Johnson, F. M.
CS Environmental Toxicology Program, Toxicology Operations Branch, National Institute of Environmental Health Sciences, Research Triangle Park, NC, 27709, USA
SO Environmental and Molecular Mutagenesis (1999), 34(4), 234-245
CODEN: EMMUEG; ISSN: 0893-6692
PB Wiley-Liss, Inc.
DT Journal
LA English
IT **13552-44-8**, 4,4'-Methylenedianiline dihydrochloride
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenic chem.-response fingerprint for male F344 rats exposed to a series of 195 chems. and implications for predicting carcinogens with transgenic models)
RN 13552-44-8 CAPLUS
CN Benzenamine, 4,4'-methylenebis-, dihydrochloride (9CI) (CA INDEX NAME)

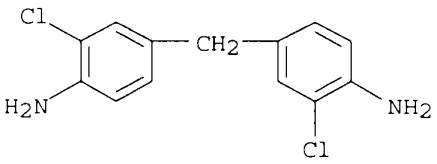


●2 HCl

AB Transgenic model systems have recently been advocated as replacements for traditional methods of testing chems. for carcinogenicity in rodents. To shed light on the diversity of responses induced by chems. in natural whole animal systems, a type of "fingerprint" is devised and, in turn, applied to describe the results of testing approx. 200 chems. in male F344 rats. Such focus helps develop an appreciation of the complexity involved in the chem. carcinogenic response. When it is asked transgenic systems to serve as replacements for natural whole animals, for predicting the risk of chem. induced **cancer**, it is being asked somehow to reflect or express this complexity so that the effects of exposure in humans can be realistically appraised. For the fingerprint, a graphic data display is used to represent the different tissues and organs that show statistically significant, chem. related tumor increases. Chems. vary extensively according to the particular sites and the array of sites that display a carcinogenic response; but any given site may also show a carcinogenic response to a variety of different chems. The data suggest that a large no. of different genetic factors may underlie the detn. of the chem. carcinogenic response. This apparent genotypic variability and complexity in phenotypic expression would seem to make it quite difficult, if not impossible, to decide on the specific performance requirements of transgenic systems for detecting carcinogens. Unless this and other

obstacles can be overcome, the transgenic approach to identifying carcinogenic chems. for regulatory purposes may best be abandoned.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1999:534929 CAPLUS
DN 131:333302
TI Qualitative and quantitative procedures for health risk assessment
AU Lohman, P. H. M.
CS Medical Genetic Center South-West the Netherlands, Department of Radiation Genetics and Chemical Mutagenesis, Leiden University Medical Center, Leiden, 2333 AL, Neth.
SO Mutation Research (1999), 428(1,2), 237-254
CODEN: MUREAV; ISSN: 0027-5107
PB Elsevier Science B.V.
DT Journal
LA English
IT **101-14-4**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(qual. and quant. procedures for health risk assessment)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



AB Numerous reactive mutagenic electrophiles are present in the environment or are formed in the human body through metabolizing processes. Those electrophiles can directly react with DNA and are considered to be ultimate carcinogens. In the past decades more than 200 in vitro and in vivo genotoxic tests have been described to identify, monitor and characterize the exposure of humans to such agents. When the responses of such genotoxic tests are quantified by a wt.-of-evidence anal., it is found that the intrinsic potency of electrophiles being mutagens does not differ much for the majority of the agents studied. Considering the fact that under normal environmental circumstances human are exposed to low concn. of about a million electrophiles, the relation between exposure to such agents and adverse health effects (e.g., **cancer**) will become a 'Pandora's box'. For quant. risk assessment it will be necessary not only to detect whether the agent is genotoxic, but also understand the mechanism of interaction of the agent with the DNA in target cells needs to be taken into account. Examples are given for a limited group of important environmental and carcinogenic agents for which such an approach is feasible. The groups identified are agents that form cross-links with DNA or are mono-alkylating agents that react with base-moieties in the DNA strands. Quant. hazard ranking of the mutagenic potency of these groups of chem. can be performed and there is ample evidence that such a ranking corresponds with the individual carcinogenic potency of those agents in rodents. Still, in practice, with the exception of certain occupational or accidental exposure situations, these approaches have not be successful in preventing **cancer** death in the human population. However,

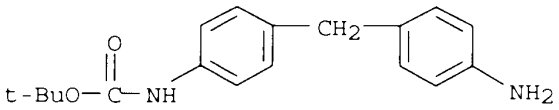
				US 1997-995750 A 19971222
				WO 1998-US26080W 19981222
EP 1041982	A1	20001011	EP 1998-964709	19981222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
				US 1997-995750 A 19971222
				WO 1998-US26080W 19981222
JP 2001526223	T2	20011218	JP 2000-525102	19981222
				US 1997-995750 A 19971222
				WO 1998-US26080W 19981222

OS MARPAT 131:87909

IT **135680-03-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of substituted heterocyclic ureas for treatment of p38 kinase-mediated diseases other than **cancer**)

RN 135680-03-4 CAPLUS

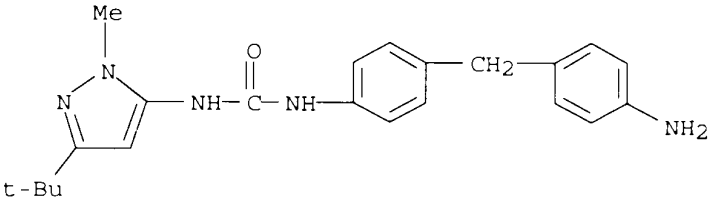
CN Carbamic acid, [4-[(4-aminophenyl)methyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT **229002-05-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of p38 kinase-mediated diseases other than **cancer**)

RN 229002-05-5 CAPLUS

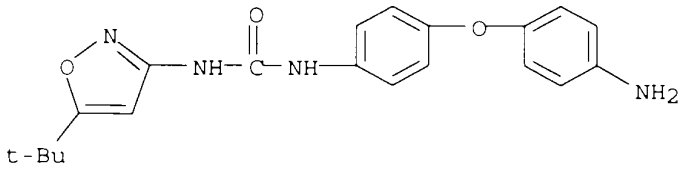
CN Urea, N-[4-[(4-aminophenyl)methyl]phenyl]-N'-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]- (9CI) (CA INDEX NAME)



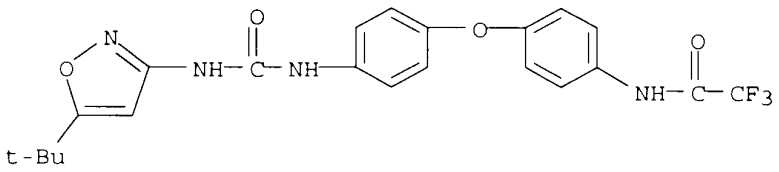
IT **228999-56-2P 228999-84-6P 229002-03-3P**
229002-04-4P 229002-06-6P 229002-07-7P
229002-08-8P 229002-09-9P 229002-11-3P
229002-24-8P 229003-25-2P 229154-78-3P
229154-79-4P 229154-94-3P 229155-42-4P
229155-43-5P 229155-44-6P 229155-45-7P
229155-46-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of p38 kinase-mediated diseases other than **cancer**)

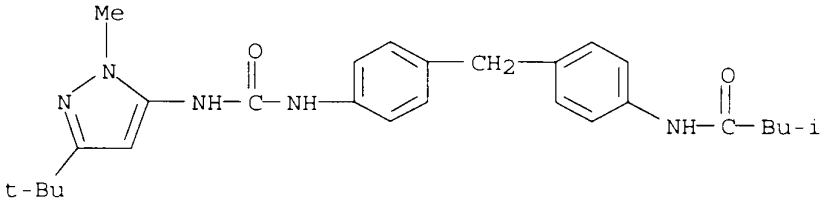
RN 228999-56-2 CAPLUS
CN Urea, N-[4-(4-aminophenoxy)phenyl]-N'-[5-(1,1-dimethylethyl)-3-isoxazolyl]- (9CI) (CA INDEX NAME)



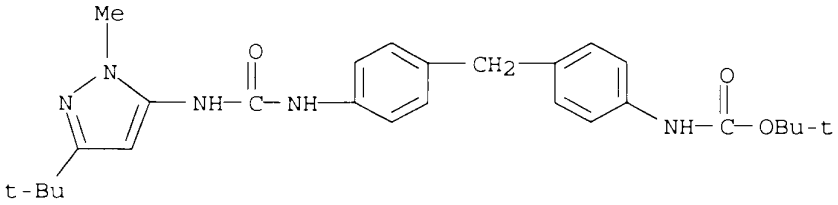
RN 228999-84-6 CAPLUS
CN Acetamide, N-[4-[4-[[[[5-(1,1-dimethylethyl)-3-isoxazolyl]amino]carbonyl]amino]phenoxy]phenyl]-2,2,2-trifluoro- (9CI) (CA INDEX NAME)



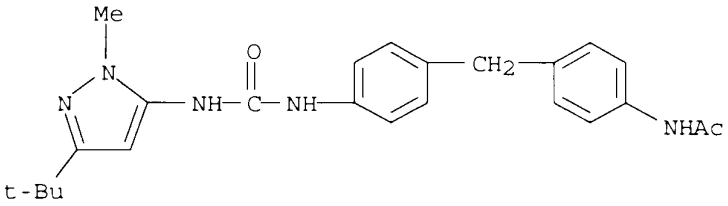
RN 229002-03-3 CAPLUS
CN Butanamide, N-[4-[[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenyl]methyl]phenyl]-3-methyl- (9CI) (CA INDEX NAME)



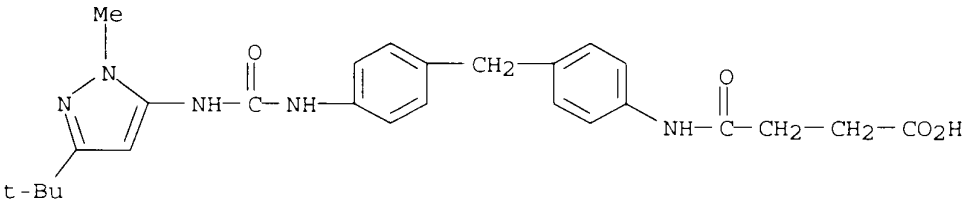
RN 229002-04-4 CAPLUS
CN Carbamic acid, [4-[[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenyl]methyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



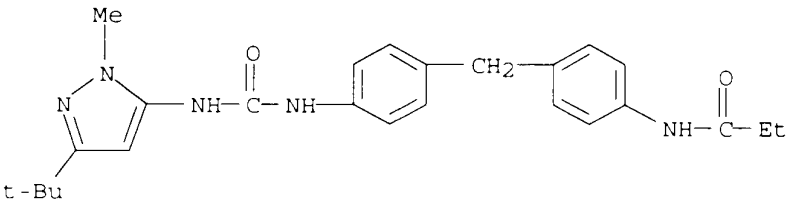
RN 229002-06-6 CAPLUS
CN Acetamide, N-[4-[[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenyl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 229002-07-7 CAPLUS
CN Butanoic acid, 4-[[4-[[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenyl]methyl]phenyl]amino]-4-oxo- (9CI) (CA INDEX NAME)

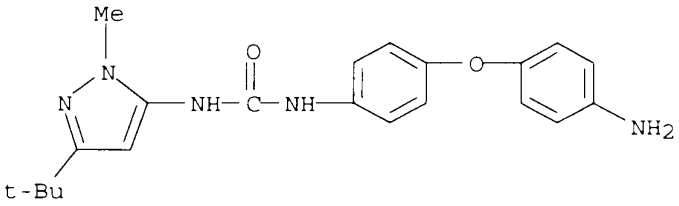


RN 229002-08-8 CAPLUS
CN Propanamide, N-[4-[[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenyl]methyl]phenyl]- (9CI) (CA INDEX NAME)

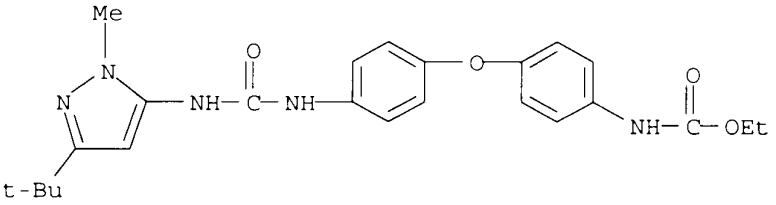


RN 229002-09-9 CAPLUS
CN Urea, N-[4-(4-aminophenoxy)phenyl]-N'-[3-(1,1-dimethylethyl)-1-methyl-1H-

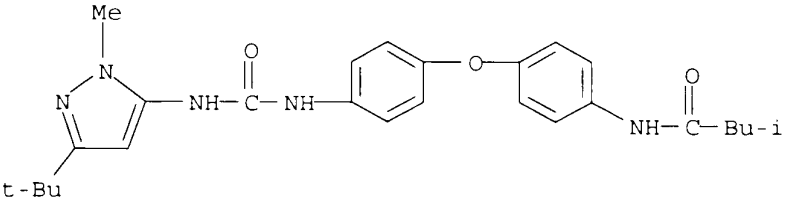
pyrazol-5-yl]- (9CI) (CA INDEX NAME)



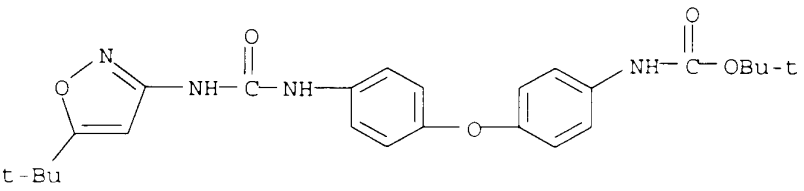
RN 229002-11-3 CAPLUS
CN Carbamic acid, [4-[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenoxy]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



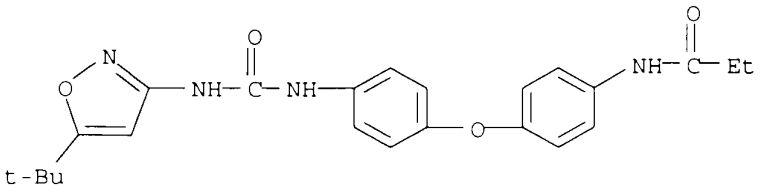
RN 229002-24-8 CAPLUS
CN Butanamide, N-[4-[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenoxy]phenyl]-3-methyl- (9CI) (CA INDEX NAME)



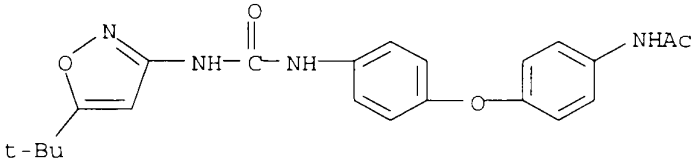
RN 229003-25-2 CAPLUS
CN Carbamic acid, [4-[4-[[[[5-(1,1-dimethylethyl)-3-isoxazolyl]amino]carbonyl]amino]phenoxy]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



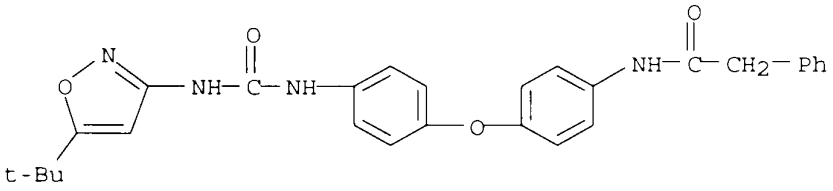
RN 229154-78-3 CAPLUS
CN Propanamide, N-[4-[4-[[[[5-(1,1-dimethylethyl)-3-isoxazolyl]amino]carbonyl]amino]phenoxy]phenyl]- (9CI) (CA INDEX NAME)



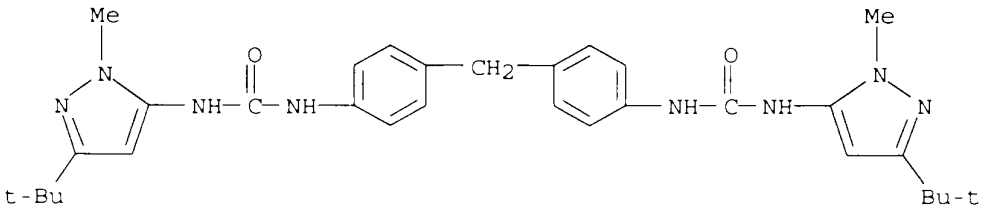
RN 229154-79-4 CAPLUS
CN Acetamide, N-[4-[4-[[[[5-(1,1-dimethylethyl)-3-isoxazolyl]amino]carbonyl]amino]phenoxy]phenyl]- (9CI) (CA INDEX NAME)



RN 229154-94-3 CAPLUS
CN Benzeneacetamide, N-[4-[4-[[[[5-(1,1-dimethylethyl)-3-isoxazolyl]amino]carbonyl]amino]phenoxy]phenyl]- (9CI) (CA INDEX NAME)

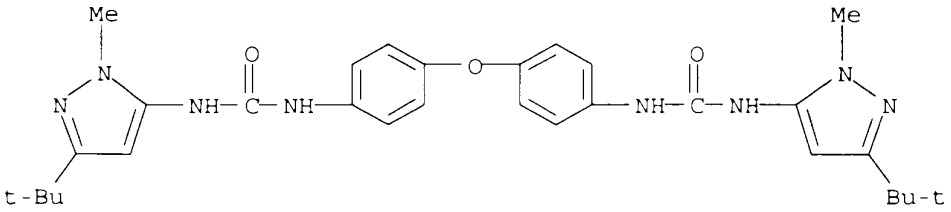


RN 229155-42-4 CAPLUS
CN Urea, N,N''-(methylenedi-4,1-phenylene)bis[N'-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]- (9CI) (CA INDEX NAME)

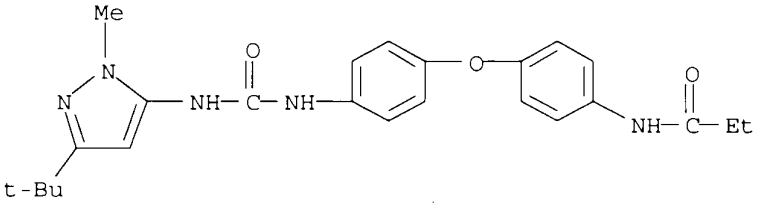


RN 229155-43-5 CAPLUS
CN Urea, N,N''-(oxydi-4,1-phenylene)bis[N'-[3-(1,1-dimethylethyl)-1-methyl-1H-

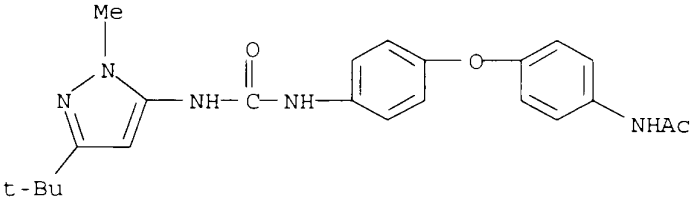
pyrazol-5-yl]- (9CI) (CA INDEX NAME)



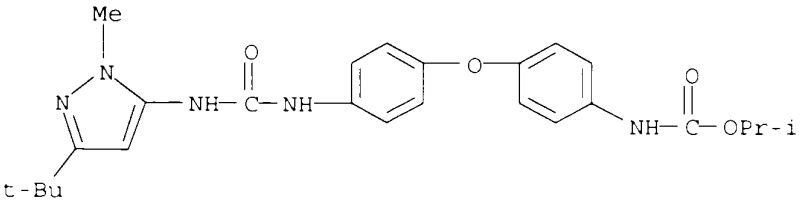
RN 229155-44-6 CAPLUS
CN Propanamide, N-[4-[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenoxy]phenyl]- (9CI) (CA INDEX NAME)



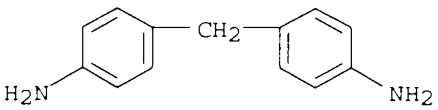
RN 229155-45-7 CAPLUS
CN Acetamide, N-[4-[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenoxy]phenyl]- (9CI) (CA INDEX NAME)



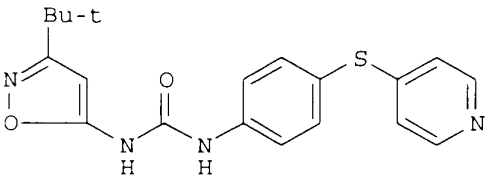
RN 229155-46-8 CAPLUS
CN Carbamic acid, [4-[4-[[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]amino]phenoxy]phenyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)



IT **101-77-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of substituted heterocyclic ureas for treatment of p38 kinase-mediated diseases other than **cancer**)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



GI



II

AB A method for treatment of p38-mediated disease other than **cancer** comprises administration of ANHCONHB [I; A = substituted isoxazolyl, pyrazolyl, thienyl, furyl; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. .gtoreq.1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-(4-pyridinylthio)aniline with 3-tert-butyl-5-isoxazolyl isocyanate in toluene gave title compd. II. In an in vitro p38 kinase assay, I displayed IC50 values of 1-10 .mu.M.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1999:421667 CAPLUS
DN 131:58659
TI Preparation of diaryl ureas as inhibitors of p38 kinase.
IN Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Hatoum-Mokdad, Holia; Rodriguez, Mareli; Sibley, Robert; Wang, Ming
PA Bayer Corporation, USA
SO PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9932463	A1	19990701	WO 1998-US27265	19981222

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,

TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 1997-995749 A 19971222

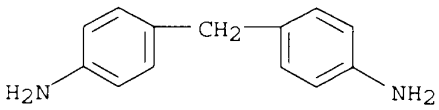
CA 2315715	AA	19990701	CA 1998-2315715 19981222
			US 1997-995749 A 19971222
			WO 1998-US27265W 19981222
AU 9919399	A1	19990712	AU 1999-19399 19981222
			US 1997-995749 A 19971222
			WO 1998-US27265W 19981222
EP 1042305	A1	20001011	EP 1998-964221 19981222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
			US 1997-995749 A 19971222
			WO 1998-US27265W 19981222
JP 2001526276	T2	20011218	JP 2000-525400 19981222
			US 1997-995749 A 19971222
			WO 1998-US27265W 19981222

OS MARPAT 131:58659

IT **101-77-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of diaryl ureas as inhibitors of p38 kinase)

RN 101-77-9 CAPLUS

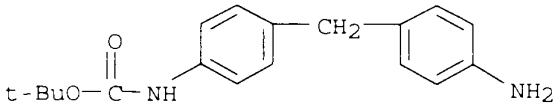
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



IT **135680-03-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of diaryl ureas as inhibitors of p38 kinase)

RN 135680-03-4 CAPLUS

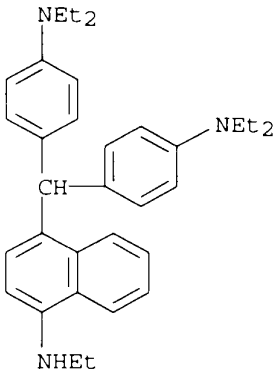
CN Carbamic acid, [4-[(4-aminophenyl)methyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



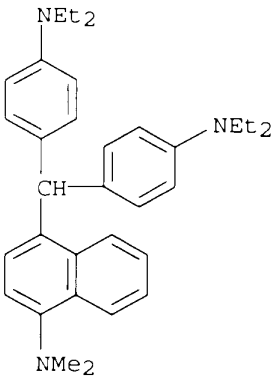
AB A method of treating a p-38 mediated disease other than **cancer** comprises administration of BNHCONHA [A = (substituted) Ph, pyridyl, 2-thienyl; B = (substituted) aryl, heteroaryl contg. .gtoreq.1 6-membered arom. structure contg. 0-4 N, O, or S atoms]. Thus, 5-tert-butyl-2-(3-tetrahydrofuranyloxy)aniline (prepn. given) and p-tolyl isocyanate were stirred 8 h in PhMe to give 75% N-(5-tert-butyl-2-(3-tetrahydrofuranyloxy)phenyl)-N'-(4-methylphenyl)urea. Title compds. inhibited p38 kinase with IC50 = 1-10 .mu.M.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

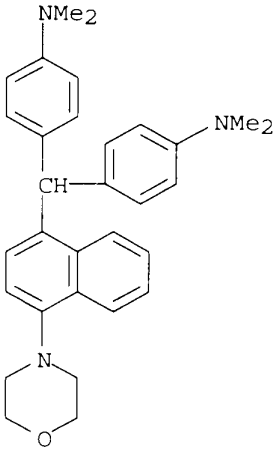
L8 ANSWER 28 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1999:352929 CAPLUS
DN 131:167168
TI Uptake and cell-killing activities of a series of Victoria blue derivatives in a mouse mammary tumor cell line
AU Wainwright, Mark; Burrow, Shuna M.; Guinot, Stephane G. R.; Phoenix, David A.; Waring, Jack
CS Dept. of Chemistry, University of Central Lancashire, Preston, PR1 2 HE, UK
SO Cytotechnology (1999), 29(1), 35-43
CODEN: CYTOER; ISSN: 0920-9069
PB Kluwer Academic Publishers
DT Journal
LA English
IT **72987-55-4 202983-70-8 202983-75-3**
239136-57-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Victoria blue derivs. uptake and cytotoxicity in breast **cancer**
)
RN 72987-55-4 CAPLUS
CN 1-Naphthalenamine, 4-[bis[4-(diethylamino)phenyl]methyl]-N-ethyl- (9CI) (CA INDEX NAME)



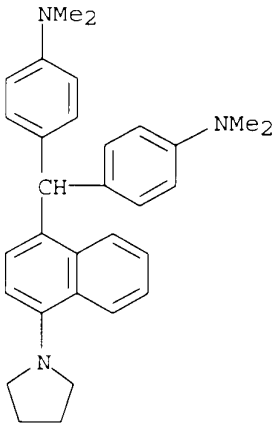
RN 202983-70-8 CAPLUS
CN 1-Naphthalenamine, 4-[bis[4-(diethylamino)phenyl]methyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 202983-75-3 CAPLUS
CN Benzenamine, 4,4'-[[4-(4-morpholinyl)-1-naphthalenyl]methylene]bis[N,N-dimethyl- (9CI) (CA INDEX NAME)



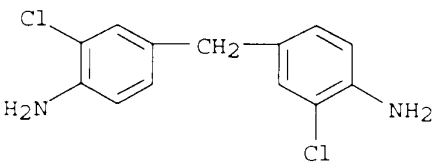
RN 239136-57-3 CAPLUS
CN Benzenamine, 4,4'-[[4-(1-pyrrolidinyl)-1-naphthalenyl]methylene]bis[N,N-dimethyl- (9CI) (CA INDEX NAME)

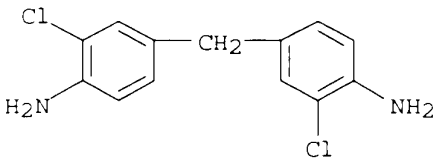


AB The triarylmethane dye Victoria blue BO (VBBO) is a known photosensitizer which has been shown to induce a cytotoxic response in vitro. Several novel Victoria blue derivs., with varying physicochem. properties, have been compared to VBBO, with respect both to dark toxicity and phototoxicity, on a mouse mammary tumor cell line, EMT6. Photosensitizer uptake was obsd. using confocal fluorescence microscopy. The chem. differences, particularly in the naphthyl substitution of the derivs. were shown to alter the light:dark toxicity differential and the uptake of the photosensitizers.

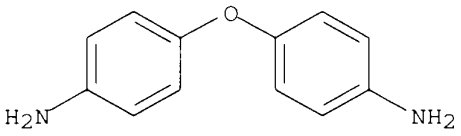
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 29 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1999:310807 CAPLUS
DN 131:69370
TI Computer-aided analysis of mutagenicity and cell transformation data for assessing their relationship with carcinogenicity
AU Taningher, Maurizio; Malacarne, Davide; Perrotta, Alessandra; Parodi, Silvio
CS Department of Clinical and Experimental Oncology, University of Genoa and National Cancer Institute, Genoa, I-16132, Italy
SO Environmental and Molecular Mutagenesis (1999), 33(3), 226-239
CODEN: EMMUEG; ISSN: 0893-6692
PB Wiley-Liss, Inc.
DT Journal
LA English
IT **101-14-4 101-80-4 13552-44-8**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(computer-aided anal. of mutagenicity and cell transformation data for assessing their relationship with carcinogenicity)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)

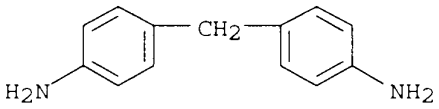




RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



RN 13552-44-8 CAPLUS
CN Benzenamine, 4,4'-methylenebis-, dihydrochloride (9CI) (CA INDEX NAME)

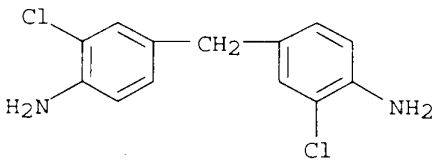


● 2 HCl

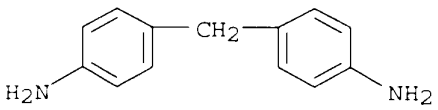
AB Using a computer-aided approach, the tests for Salmonella mutagenicity and transformation in established cell lines were compared for the qual. bases of their carcinogenicity predictions. For this purpose, a database of 145 chems. was prepd. in which rodent carcinogenicity data and results of the Ames' and transformation tests were available. Using a software program for connectivity anal. (previously developed and validated by us), the authors assayed the mol. structures of these chems. for the presence of fragments relatable to their pos. (i.e., biophores) or neg. (i.e., biophobes) response to the tests in question. These fragments were then studied for their assocn. with genotoxic and nongenotoxic carcinogenicity. The philosophy adopted was that the type and no. of mol. fragments chosen by the software to describe the chems. correctly predicted by the tests could be related to the type of carcinogenic effects to which the tests themselves were sensitive. The classifications made by the software were interpreted by human expertise and the biophores found were compared with the acknowledged structural alerts to DNA reactivity as formalized by Ashby and co-workers [(1991): Mutat Res 257:229-306; (1993): Mutat Res 286:3-74]. The results show that, in quant. terms, the overall ability to predict carcinogenicity is about the same for both the Salmonella and transformation tests. However, in qual. terms the transformation test appears to be sensitive to effects that are more heterogeneous than those inducing mutation, some of which are presumably related to nongenotoxic carcinogenic activities. This study illustrates a possible, innovative model of anal. of chem. structures that, using an automated approach along with the biologist's judgment, could contribute to the detection of

complementarities among short-term test endpoints.
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

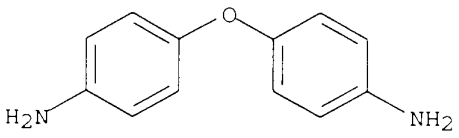
L8 ANSWER 30 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1999:212389 CAPLUS
DN 131:28695
TI The alkaline single cell gel electrophoresis assay with mouse multiple organs: results with 30 aromatic amines evaluated by the IARC and U.S. NTP
AU Sasaki, Yu F.; Fujikawa, Keiko; Ishida, Kumiko; Kawamura, Noriko; Nishikawa, Yukiko; Ohta, Shigenori; Satoh, Mana; Madarame, Hiroo; Ueno, Shunji; Susa, Nobuyuki; Matsusaka, Naonori; Tsuda, Shuji
CS Faculty of Chemical and Biological Engineering, Laboratory of Genotoxicity, Hachinohe National College of Technology, Hachinohe, Aomori, 039-11, Japan
SO Mutation Research (1999), 440(1), 1-18
CODEN: MUREAV; ISSN: 0027-5107
PB Elsevier Science B.V.
DT Journal
LA English
IT **101-14-4 101-77-9 101-80-4 139-65-1**,
4,4'-Thiodianiline
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(arom. amines genotoxicity detd. by alk. single cell gel electrophoresis assay with multiple organs)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



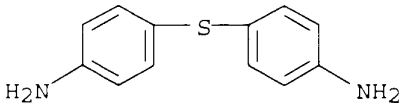
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



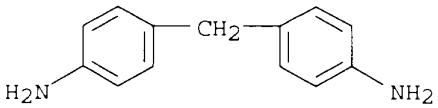
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



AB The genotoxicity of 30 arom. amines selected from IARC (International Agency for Research on **Cancer**) groups 1, 2A, 2B and 3 and from the U.S. NTP (National Toxicol. Program) carcinogenicity database were evaluated using the alk. single cell gel electrophoresis (SCG) (Comet) assay in mouse organs. We treated groups of four mice once orally at the max. tolerated dose (MTD) and sampled stomach, colon, liver, kidney, bladder, lung, brain, and bone marrow 3, 8 and 24 h after treatment. For the 20 arom. amines that are rodent carcinogens, the assay was pos. in at least one organ, suggesting a high predictive ability for the assay. For most of the SCG-pos. arom. amines, the organs exhibiting increased levels of DNA damage were not necessarily the target organs for carcinogenicity. It was rare, in contrast, for the target organs not to show DNA damage. Organ-specific genotoxicity, therefore, is necessary but not sufficient for the prediction of organ-specific carcinogenicity. For the 10 non-carcinogenic arom. amines (eight were Ames test-pos. and two were Ames test-neg.), the assay was neg. in all organs studied. In the safety evaluation of chems., it is important to demonstrate that Ames test-pos. agents are not genotoxic in vivo. Chem. carcinogens can be classified as genotoxic (Ames test-pos.) and putative non-genotoxic (Ames test-neg.) carcinogens. The alk. SCG assay, which detects DNA lesions, is not suitable for identifying non-genotoxic carcinogens. The present SCG study revealed a high pos. response ratio for rodent genotoxic carcinogens and a high neg. response ratio for rodent genotoxic non-carcinogens. These results suggest that the alk. SCG assay can be usefully used to evaluate the in vivo genotoxicity of chems. in multiple organs, providing for a good assessment of potential carcinogenicity.
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 31 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1998:281284 CAPLUS
DN 128:274337
TI Application of health information to hazardous air pollutants modeled in EPA's cumulative exposure project
AU Caldwell, Jane C.; Woodruff, Tracey J.; Morello-Frosch, Rachel; Axelrad, Daniel A.
CS Office of Air and Radiation, Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC, 27711, USA
SO Toxicology and Industrial Health (1998), 14(3), 429-454
CODEN: TIHEEC; ISSN: 0748-2337
PB Princeton Scientific Publishing Co., Inc.
DT Journal
LA English
IT **101-77-9**
RL: ADV (Adverse effect, including toxicity); POL (Pollutant); BIOL (Biological study); OCCU (Occurrence)
(application of health information to hazardous air pollutants modeled

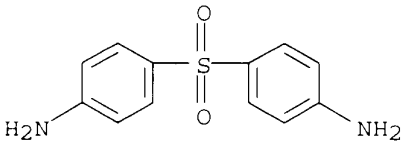
in EPA's cumulative exposure project)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



AB Relatively little is known about the spectrum of health effects, and the scope and level of ambient air concns. of those pollutants regulated under the Clean Air Act as "hazardous air pollutants.". The U.S. Environmental Protection Agency's (USEPA) Cumulative Exposure Project uses currently available emissions inventories, from a variety of source types, and an atm. dispersion model to provide ests. of ambient concns. for 148 hazardous air pollutants (HAPs) in over 60,000 census tracts for the year 1990. This paper uses currently available hazard information for those pollutants and provides a database of potential regulatory threshold concns. of concern, or "benchmark concns.," and a methodol. for prioritizing and characterizing the quality of the data. In order to demonstrate application of the database and prioritization scheme to outputs from the Cumulative Exposure Project, comparisons were made with the max. modeled concn. of each individual hazardous air pollutant across the census tracts. Of the 197 benchmark concns. for **cancer** and non-**cancer** (long- and short-term exposures) effects compiled for the study, approx. one half were exceeded with a predominance of exceedance of **cancer** benchmarks. While the no. of benchmark concns. available to fully characterize potential health effects of these pollutants was limited (approx. 80 percent of HAPs identified as **cancer** concerns had benchmark concns. for **cancer** and 50 percent of all HAPs had non-**cancer** benchmark concns.) and there was greater uncertainty in derivation of max. modeled air concns. than other levels, the comparison between the two was a useful approach for providing an indication of public health concern from hazardous air pollutants.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

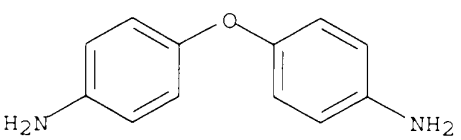
L8 ANSWER 32 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1998:56110 CAPLUS
DN 128:110473
TI All-trans-retinoic acid modulation of drug-metabolizing enzyme activities. Investigation with selective metabolic drug probes
AU Adedoyin, Adedayo; Stiff, Dwight D.; Smith, David C.; Romkes, Marjorie; Bahnson, Robert C.; Day, Roger; Hofacker, Janie; Branch, Robert A.; Trump, Donald L.
CS Center Clinical Pharmacology, Medical Center, University Pittsburgh, Pittsburgh, PA, 15213, USA
SO Cancer Chemotherapy and Pharmacology (1998), 41(2), 133-139
CODEN: CCPHDZ; ISSN: 0344-5704
PB Springer-Verlag
DT Journal
LA English
IT **80-08-0**, Dapsone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(N-acetyltransferase activity after ATRA treatment in

hormone-refractory prostate **cancer**)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)

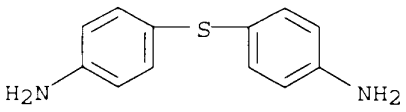


AB In the course of a phase II evaluation of all-trans-retinoic acid (ATRA) in prostate **cancer**, the activities of 5 specific cytochrome P 450 (CYP) (CYPs 1A2, 2C19, 2D6, 2E1, and 3A4) and N-acetyltransferase enzymes were investigated, using a newly developed 5-drug cocktail involving caffeine, mephenytoin, debrisoquine, chlorzoxazone, and dapsone resp. Enzyme activities were assessed in patients with hormone-refractory prostate **cancer** before the initiation of ATRA therapy, after 14 days of continuous ATRA administration, and 7 days after cessation of drug therapy. After 14 days of ATRA therapy, the activities of CYP 2E1 (chlorzoxanzone hydrolase) and N-acetyltransferase (in fast acetylators only) were increased by 83 and 29% resp. Both activities returned to baseline by 7 days after cessation of therapy and the profiles were similar to the changes seen in the clearance of ATRA itself.

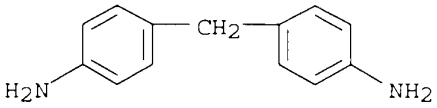
L8 ANSWER 33 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1997:424064 CAPLUS
DN 127:77218
TI T25: a simplified carcinogenic potency index: description of the system and study of correlations between carcinogenic potency and species/site specificity and mutagenicity
AU Dybing, Erik; Sanner, Tore; Roelfzema, Henk; Kroese, Dinant; Tennant, Raymond W.
CS Department of Environmental Medicine, National Institute of Public Health, Oslo, 0403, Norway
SO Pharmacology & Toxicology (Copenhagen) (1997), 80(6), 272-279
CODEN: PHTOEH; ISSN: 0901-9928
PB Munksgaard
DT Journal
LA English
IT **101-80-4**, 4,4'-Oxydianiline **139-65-1**, 4,4'-Thiodianiline **13552-44-8**, 4,4'-Methylenedianiline dihydrochloride
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(T25, simplified carcinogenic potency index and study of correlations between carcinogenic potency and species/site specificity and mutagenicity)
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



RN 13552-44-8 CAPLUS
CN Benzenamine, 4,4'-methylenebis-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

AB A simplified carcinogenic potency index, the T25, is proposed as a practical method for the inclusion of potency considerations in carcinogen classification systems. The T25 is the chronic daily dose in mg per kg bodyweight which will give 25% of the animals tumors at a specific tissue site, after correction for spontaneous incidence, within the std. life span of that species. Calcd. T25 values of a set of 113 US National **Cancer** Institute/National Toxicol. Program (NC/NTP) carcinogens showed excellent correlation (correlation coeff. 0.96) with the carcinogenic potency index TD50 of R. Peto et al. (1984). The mean of T25 values for 51 transspecies, multiple common site NCI/NTP carcinogens were 10-fold lower than those for 62 NCI/NTP single species, single site carcinogens. For these 113 carcinogens, the mean T25 values were approx. 3-fold lower for agents that were also mutagenic in Salmonella compared to the nonmutagenic agents.

L8 ANSWER 34 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1997:361626 CAPLUS
DN 126:330493
TI Sulfoxide derivatives of nitrogen-mustard and anticancer agent containing the same
IN Kim, Jung Woo; Kwon, Chul-Hoon; Chung, Koo Hun; Kim, Joon Kyum; Shin, Jae Soo; Min, Kwan Kee
PA Chong Kun Dang Corp., S. Korea; Kim, Jung Woo; Kwon, Chul-Hoon; Chung, Koo Hun; Kim, Joon Kyum; Shin, Jae Soo; Min, Kwan Kee
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9713748	A1	19970417	WO 1996-KR173	19961009

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KZ, LK, LR, LS, LT,

LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN

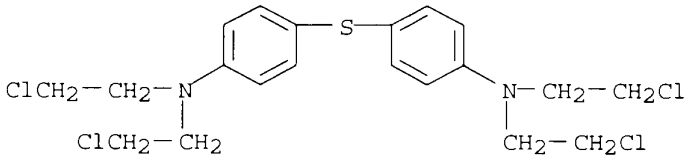
				KR 1995-34486	19951009
AU 9673406	A1	19970430		AU 1996-73406	19961009
				KR 1995-34486	19951009
				WO 1996-KR173	19961009

OS MARPAT 126:330493

IT **189639-02-9P**, N,N,N',N'-Tetrakis(2-chloroethyl)-4,4'-dianiline sulfide **189639-03-0P**, N,N'-Bis(2-chloroethyl)-4,4'-dianiline sulfide **189639-04-1P**, 4-[N,N-Bis(2-chloroethyl)amino]-4'-(9-acridinylamino)diphenyl sulfide hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(intermediate and drug; prepn. of sulfoxide derivs. of nitrogen-mustards as anticancer agent prodrugs for hypoxic tumors)

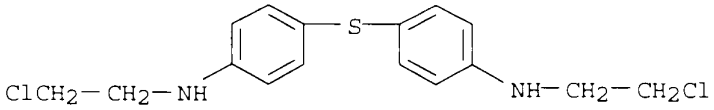
RN 189639-02-9 CAPLUS

CN Benzenamine, 4,4'-thiobis[N,N-bis(2-chloroethyl)- (9CI) (CA INDEX NAME)



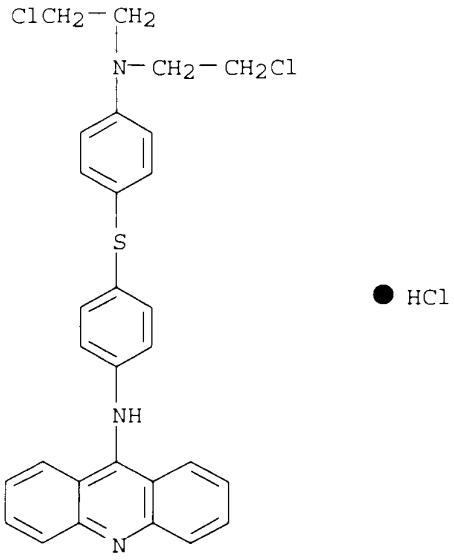
RN 189639-03-0 CAPLUS

CN Benzenamine, 4,4'-thiobis[N-(2-chloroethyl)- (9CI) (CA INDEX NAME)



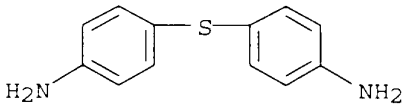
RN 189639-04-1 CAPLUS

CN 9-Acridinamine, N-[4-[[4-[bis(2-chloroethyl)amino]phenyl]thio]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

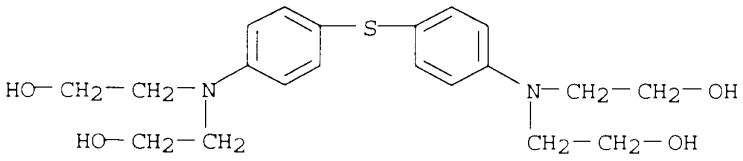


IT **139-65-1P 189639-06-3P**, N,N,N',N'-Tetrakis(2-hydroxyethyl)-4,4'-dianiline sulfide **189639-07-4P**, N,N'-Bis(2-hydroxyethyl)-4,4'-dianiline sulfide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of sulfoxide derivs. of nitrogen-mustards as anticancer agent prodrugs for hypoxic tumors)

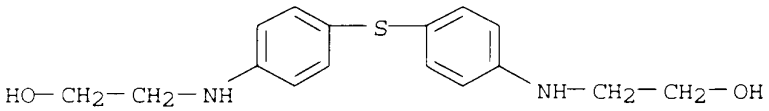
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



RN 189639-06-3 CAPLUS
CN Ethanol, 2,2',2'',2'''-[thiobis(4,1-phenylenenitrilo)]tetrakis- (9CI) (CA INDEX NAME)

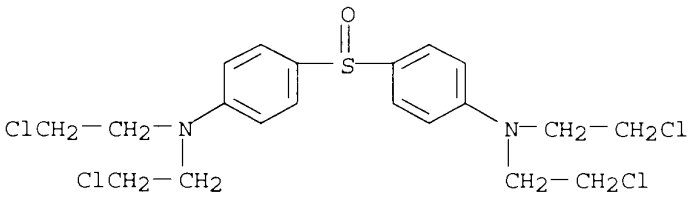


RN 189639-07-4 CAPLUS
CN Ethanol, 2,2'-[thiobis(4,1-phenyleneimino)]bis- (9CI) (CA INDEX NAME)

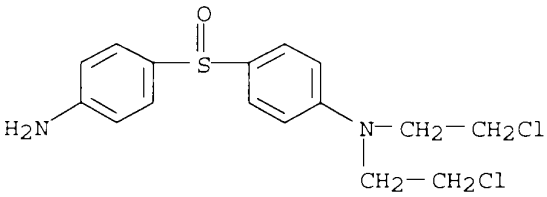


IT **189638-97-9P**, N,N,N',N'-Tetrakis(2-chloroethyl)-4,4'-dianiline sulfoxide **189639-00-7P**, 4-[N,N-Bis(2-chloroethyl)amino]-4'-aminodiphenyl sulfoxide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(target prodrug; prepn. of sulfoxide derivs. of nitrogen-mustards as anticancer agent prodrugs for hypoxic tumors)

RN 189638-97-9 CAPLUS
CN Benzenamine, 4,4'-sulfinylbis[N,N-bis(2-chloroethyl)- (9CI) (CA INDEX NAME)

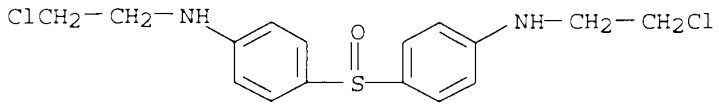


RN 189639-00-7 CAPLUS
CN Benzenamine, 4-[(4-aminophenyl)sulfinyl]-N,N-bis(2-chloroethyl)- (9CI) (CA INDEX NAME)

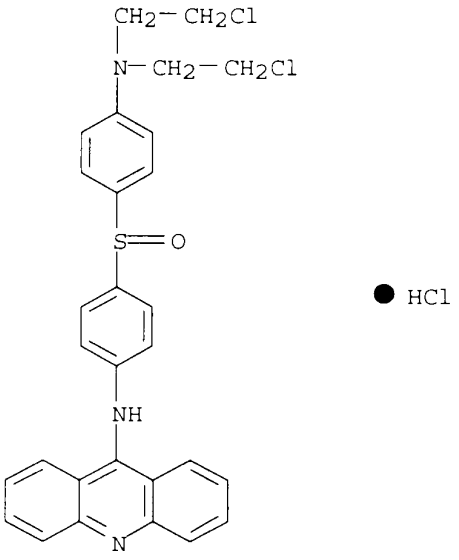


IT **189638-98-0P**, N,N'-Bis(2-chloroethyl)-4,4'-dianiline sulfoxide **189639-01-8P**, 4-[N,N-Bis(2-chloroethyl)amino]-4'-(9-acridinylamino)diphenyl sulfoxide hydrochloride
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(target prodrug; prepn. of sulfoxide derivs. of nitrogen-mustards as anticancer agent prodrugs for hypoxic tumors)

RN 189638-98-0 CAPLUS
CN Benzenamine, 4,4'-sulfinylbis[N-(2-chloroethyl)- (9CI) (CA INDEX NAME)

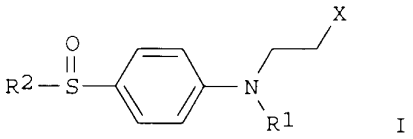


RN 189639-01-8 CAPLUS
CN 9-Acridinamine, N-[4-[[4-[bis(2-chloroethyl)amino]phenyl]sulfinyl]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

GI

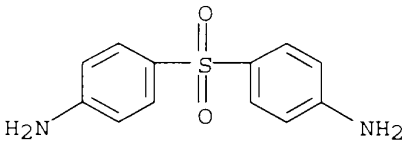


I

AB The invention provides sulfoxide derivs. of nitrogen-mustard, with general formula I [R1 = H or haloethyl; R2 = (un)substituted alkyl or Ph; X = halo; provided that R1 = chloroethyl and X = Cl, then R2 .noteq. Me]. Also provided are anticancer agents comprising I as prodrugs. I convert to highly cytotoxic sulfides under hypoxic conditions, and thus are very useful as anticancer agents which selectively act on solid **cancers** which are in a hypoxic state. For example, etherification of p-O2NC6H4SH with PrBr gave 86.3% p-O2NC6H4SPr, which was reduced with Sn in aq. HCl to give 85.6% p-H2NC6H4SPr. Bis-N-alkylation of the latter with excess ClCH2CH2OH (30.6%) and chlorination of the alc. functions with POCl3 gave the N mustard sulfide p-PrSC6H4N(CH2CH2Cl)2 (II), which was S-oxidized with H2O2 in CF3CO2H to give the title sulfoxide prodrug p-PrS(O)C6H4N(CH2CH2Cl)2 (III) in 74.3% yield. In a test against Chinese

hamster lung V-79 transformed cells, II had an IC50 value of 2.46 .mu.M/mL, while its less potent prodrug III had an IC50 of 433.9 .mu.M/mL. However, when III was administered under hypoxic conditions, the IC90 value improved from 939.2 .mu.M/mL (normal) to 290.7 .mu.M/mL.

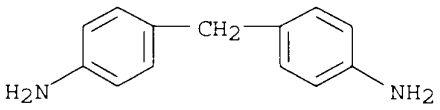
L8 ANSWER 35 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1997:301803 CAPLUS
DN 127:294
TI Effects of dual combinations of antifolates with atovaquone or dapsone on nucleotide levels in Plasmodium falciparum
AU Yeo, Anthony E. T.; Seymour, Kristen K.; Rieckmann, Karl H.; Christopherson, Richard I.
CS DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF SYDNEY, SYDNEY, NSW 2006, Australia
SO Biochemical Pharmacology (1997), 53(7), 943-950
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier
DT Journal
LA English
IT **80-08-0**, Dapsone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of dual combinations of antifolates with atovaquone or dapsone on nucleotide levels in Plasmodium falciparum)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



AB The triazine antifolates, cycloguanil and WR99210, and their parent biguanide compds., proguanil and PS-15, were tested in combination with a series of antimalarial drugs for synergism against Plasmodium falciparum growing in erythrocytic culture. Four synergistic combinations were found: cycloguanil-dapsone, WR99210-dapsone, proguanil-atovaquone, and PS-15-atovaquone. Cycloguanil-dapsone or WR99210-dapsone had a profound suppressive effect on the concn. of dTTP in parasites while that of dATP increased. Depletion of dTTP is consistent with cycloguanil or WR99210 inhibiting dihydrofolate reductase and dapsone inhibiting dihydropteroate synthase. For the combinations proguanil-atovaquone and PS-15-atovaquone, the levels of nucleoside triphosphates (NTPs) and dNTPs were generally suppressed, suggesting that inhibition is not through nucleotide pathways but probably through another metabolic mechanism(s). Combinations of two synergistic pairs of antimalarial drugs, (proguanil-atovaquone)-(cycloguanil-dapsone) and (PS-15-atovaquone)-(WR99210-dapsone), were tested, and it was found that NTPs and dNTPs decreased much more than for a single synergistic combination. Dual synergistic combinations could play an important role in the therapy of multidrug-resistant malaria, just as combination chemotherapy is used to treat **cancer**.

L8 ANSWER 36 OF 105 CAPLUS COPYRIGHT 2003 ACS

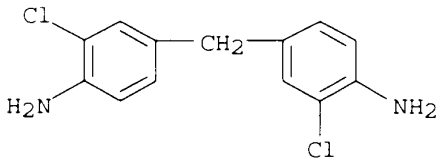
AN 1997:114657 CAPLUS
DN 126:228913
TI Detection of carcinogenic amines from dyestuffs of dyed substrates
AU Oh, S. W.; Kang, M. N.; Cho, C. W.; Lee, M. W.
CS Korea Research Institute of Chemical Technology, Taejeon, 305-606, S. Korea
SO Dyes and Pigments (1997), 33(2), 119-135
CODEN: DYPIDX; ISSN: 0143-7208
PB Elsevier
DT Journal
LA English
IT **101-77-9**, 4,4'-Diaminodiphenylmethane
RL: MSC (Miscellaneous)
(detection of carcinogenic amines from dyestuffs of dyed substrates)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



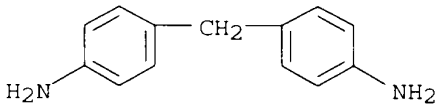
AB In this study, it was surprising to find that some dyestuffs or dyed substrates released carcinogenic amines such as 4-aminodiphenyl, 2-naphthylamine, 2,4-toluenediamine and 4,4'-diaminodiphenylmethane, although such amines had not been employed as intermediates in the manuf. of the dyestuffs. Benzidine was also detected from a dyestuff which was not made from benzidine. The 2-naphthylamine residues were sourced as being due to the use of 1-naphthylamine contaminated with 2-naphthylamine. Dediazoniation and a subsequent coupling reaction between the benzenediazonium ion and aniline was responsible for the formation of 4-aminodiphenyl. Benzidine was derived from dediazoniation and a subsequent self-coupling reaction of the diazonium ion of 4-nitroaniline. 2,4-Toluenediamine and 4,4'-diaminodiphenylmethane arose from the alk. hydrolysis of the readily accessible moiety of the corresponding base units in PU foams or PU finishing agents.

L8 ANSWER 37 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1997:93197 CAPLUS
DN 126:153876
TI Evaluation of the rodent micronucleus assay in the screening of IARC carcinogens (Groups 1, 2A and 2B). The summary report of the 6th collaborative study by CSGMT/JEMS.cntdot.MMS
AU Morita, Takeshi; Asano, Norihide; Awogi, Takumi; Sasaki, Yu F.; Sei-ichi Sato; Shimada, Hiroyasu; Sutou, Sizuyo; Suzuki, Takayoshi; Akihiro Wakata; Sofuni, Toshio; Hayashi, Makoto
CS Tsukuba Research Laboratories, Nippon Glaxo Ltd., 43 Wadai, Tsukuba, Ibaraki, 300-42, Japan
SO Mutation Research (1997), 389(1), 3-122
CODEN: MUREAV; ISSN: 0027-5107
PB Elsevier
DT Journal
LA English
IT **101-14-4**, 4,4'-Methylene bis(2-chloroaniline) **101-77-9**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogens genotoxicity as detd. by micronucleus assay)

RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



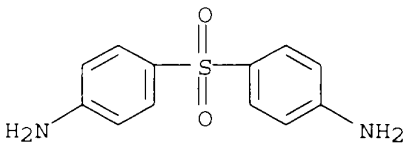
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



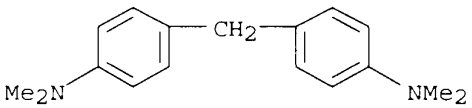
AB To assess the correlation between micronucleus induction and human carcinogenicity, the rodent micronucleus assay was performed on known and potential human carcinogens in the 6th MMS/CSGMT collaborative study. Approx. 100 com. available chems. and chem. groups on which there was little or no micronucleus assay data were selected from IARC (International Agency for Research on **Cancer**) Groups 1 (human carcinogen), 2A (probable human carcinogen) and 2B (possible human carcinogen). As min. requirements for the collaborative study, 5 male mice were treated by i.p. injection or oral gavage once or twice with each chem. at three dose levels, and bone marrow and/or peripheral blood was analyzed. Five positives and 2 inconclusives out of 13 Group 1 chems., 7 positives and 5 inconclusives of 23 Group 2A chems., and 26 positives and 6 inconclusives of 67 Group 2B chems. were found. Such low pos. rates were not surprising because of a test chem. selection bias, and we excluded well-known micronucleus inducers. The overall evaluation of the rodent micronucleus assay was based on the present data combined with published data on the IARC carcinogens. After merging, the pos. rates for Groups 1, 2A and 2B were 68.6, 54.5 and 45.6%, resp. Structure-activity relation anal. suggested that the micronucleus assay is more sensitive to the genetic toxicity of some classes of chems. Those to which it is sensitive consist of (1) aziridines and bis(2-chloroethyl) compds.; (2) alkyl sulfonate and sulfates; (3) acyl-type N-nitroso compds.; (4) hydrazines; (5) aminobiphenyl and benzidine derivs.; and (6) azo compds. Those to which it is less sensitive consist of (1) dialkyl type N-nitroso compds.; (2) silica and metals and their compds.; (3) arom. amines without other functional groups; (4) halogenated compds.; and (5) steroids and other hormones. After incorporation of structure-activity relation information, the pos. rates of the rodent micronucleus assay became 90.5, 65.2 and 60.0% for IARC Groups 1, 2A and 2B, resp. Noteworthy was the tendency of the test to be more sensitive to those carcinogens with stronger evidence human carcinogenicity.

L8 ANSWER 38 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1996:749877 CAPLUS
DN 126:43857
TI Prediction of rodent carcinogenicity bioassays from molecular structure

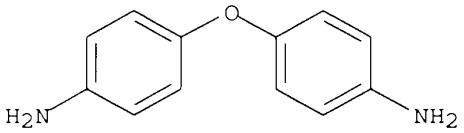
using inductive logic programming
AU King, Ross D.; Srinivasan, Ashwin
CS Biomolecular Modelling Laboratory, University Oxford, London, WC2A 3PX, UK
SO Environmental Health Perspectives Supplements (1996), 104(5), 1031-1040
CODEN: EHPSEO; ISSN: 1078-0475
PB National Institute of Environmental Health Sciences
DT Journal
LA English
IT **80-08-0 101-61-1 101-80-4 139-65-1**
13552-44-8, 4,4'-Methylenedianiline dihydrochloride
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(prediction of rodent carcinogenicity bioassays from mol. structure using inductive logic programming)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



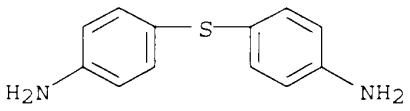
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



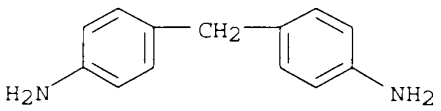
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



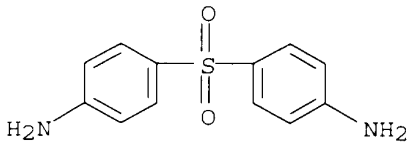
RN 13552-44-8 CAPLUS
CN Benzenamine, 4,4'-methylenebis-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

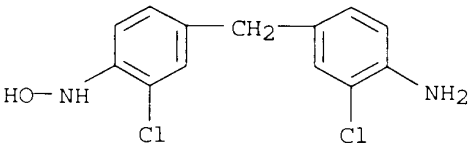
AB The machine learning program Progol was applied to the problem of forming the structure-activity relation (SAR) for a set of compds. tested for carcinogenicity in rodent bioassays by the U.S. National Toxicol. Program (NTP). Progol is the first inductive logic programming (ILP) algorithm to use a fully relational method for describing chem. structure in SARs, based on using atoms and their bond connectivities. Progol is well suited to forming SARs for carcinogenicity as it is designed to produce easily understandable rules (structural alerts) for sets of noncongeneric compds. The Progol SAR method was tested by prediction of a set of compds. that have been widely predicted by other SAR methods (the compds. used in the NTP's first round of carcinogenesis predictions). For these compds. no method (human or machine) was significantly more accurate than Progol. Progol was the most accurate method that did not use data from biol. tests on rodents (however, the difference in accuracy is not significant). The Progol predictions were based solely on chem. structure and the results of tests for Salmonella mutagenicity. Using the full NTP database, the prediction accuracy of Progol was estd. to be 63% (.+-.3%) using 5-fold cross validation. A set of structural alerts for carcinogenesis was automatically generated and the chem. rationale for them investigated-these structural alerts are statistically independent of the Salmonella mutagenicity. Carcinogenicity is predicted for the compds. used in the NTP's second round of carcinogenesis predictions. The results for prediction of carcinogenesis, taken together with the previous successful applications of predicting mutagenicity in nitroarom. compds., and inhibition of angiogenesis by suramin analogs, show that Progol has a role to play in understanding the SARs of **cancer**-related compds.

L8 ANSWER 39 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1996:703920 CAPLUS
DN 126:44275
TI Inhibition of glycosylphosphatidylinositol (GPI) phospholipase D by suramin-like compounds
AU Brunner, Georg; Zalkow, Leon; Burgess, Edward; Rifkin, Daniel B.; Wilson, E. Lynette; Gruszecka-Kowalik, Ewa; Powis, Garth
CS Medical School, New York University, New York, NY, USA
SO Anticancer Research (1996), 16(5A), 2513-2516
CODEN: ANTRD4; ISSN: 0250-7005
PB Anticancer Research
DT Journal
LA English
IT **80-08-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(inhibition of human glycosylphosphatidylinositol phospholipase D and **cancer** cell growth by suramin azo analogs)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



AB A no. of proteins are found attached to the plasma membrane of mammalian cells by a glycosylphosphatidylinositol (GPI) anchor that can be cleaved by GPI specific phospholipase D (GPI-PLD). There are no known specific inhibitors of GPI-PLD. Here, the authors examd. some inhibitors of phosphatidylinositol specific phospholipase C (PI-PLC) for their ability to inhibit human serum and human bone marrow cell GPI-PLD. Azo analogs of suramin were found to be potent inhibitors of GPI-PLD. One compd. had an IC50 of 3.7 .mu.M that was 10-fold lower than the IC50 required to inhibit PI-PLC. The azo suramin analogs inhibited **cancer** cell growth at concns. similar to those required to inhibit GPI-PLD, and below concns. required to inhibit growth factor binding. It is possible that inhibition of cell growth might be related to the ability of the compds. to inhibit GPI-PLD.

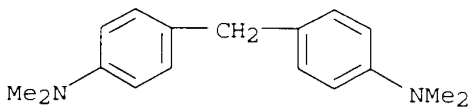
L8 ANSWER 40 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1996:274347 CAPLUS
DN 125:3364
TI Neoplastic transformation and DNA-binding of 4,4'-methylenebis(2-chloroaniline) in SV40-immortalized human uroepithelial cell lines
AU Swaminathan, Santhanam; Frederickson, Susan M.; Hatcher, James F.; Reznikoff, Catherine A.; Butler, Mary A.; Cheever, Kenneth L.; Savage, Russell E. Jr.
CS Comprehensive Cancer Center, University Wisconsin, Madison, WI, 53792, USA
SO Carcinogenesis (1996), 17(4), 857-864
CODEN: CRNGDP; ISSN: 0143-3334
PB Oxford University Press
DT Journal
LA English
IT **115084-47-4**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(neoplastic transformation and DNA-binding of methylenebis(chloroaniline) in SV40-immortalized human uroepithelial cell lines)
RN 115084-47-4 CAPLUS
CN Benzenamine, 4-[(4-amino-3-chlorophenyl)methyl]-2-chloro-N-hydroxy- (9CI) (CA INDEX NAME)



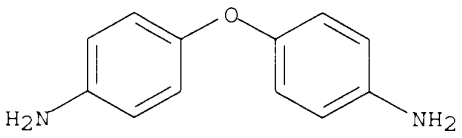
AB The tumorigenic transformation of certain occupationally significant chems., such as N-hydroxy-4,4'-methylenebis[2-chloroaniline] (N-OH-MOCA),

N-hydroxy-ortho-toluidine (N-OH-OT), 2-phenyl-1,4-benzoquinone (PBQ) and N-hydroxy-4-aminobiphenyl (N-OH-ABP) were tested in vitro using the well established SV40-immortalized human uroepithelial cell line SV-HUC.PC. SV-HUC cells were exposed in vitro to varying concn. of N-OH-MOCA, N-OH-OT, N-OH-ABP and PBQ that caused approx. 25% and 75% cytotoxicity. The carcinogen treated cells were propagated in culture for about six weeks and subsequently injected s.c. into athymic nude mice. Two of the fourteen different groups of SV-HUC.PC treated with different concns. of N-OH-MOCA, and one of the three groups exposed to N-OH-ABP, formed carcinomas in athymic nude mice. 32P-postlabelling analyses of DNA isolated from SV-HUC.PC after exposure to N-OH-MOCA revealed one major and one minor adduct. The major adduct has been identified as the N-(deoxyadenosine-3',5'-bisphospho-8-yl)-4-amino-3-chlorotoluene alc. (pdAp-ACBA) and the minor adduct as N-(deoxyadenosine-3',5'-bisphospho-8-yl)-4-amino-3-chlorotoluene (pdAp-ACT). Furthermore, SV-HUC.PC cytosols catalyzed the binding of N-OH-MOCA to DNA, in the presence of acetyl-CoA, to yield similar adducts. The same adducts were also formed by chem. interaction of N-OH-MOCA with calf thymus DNA, suggesting that the aryl nitrenium ion may be the ultimate reactive species responsible for DNA binding. The tumorigenic activity of N-OH-MOCA in this highly relevant in vitro transformation model, coupled with the findings that SV-HUC.PC cells formed DNA-adducts in vitro and contained enzyme systems that activated N-OH-MOCA to reactive electrophilic species that bound to DNA, strongly suggest that MOCA could be a human bladder carcinogen. These findings are consistent with the International Agency for Research on **Cancer** 's classification of MOCA as a probable human carcinogen.

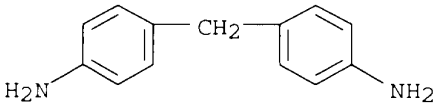
L8 ANSWER 41 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1995:803360 CAPLUS
DN 123:248848
TI Assessment of effect levels of chemicals from quantitative structure-activity relationship (QSAR) models. I. Chronic lowest-observed-adverse-effect level (LOAEL)
AU Mumtaz, M. M.; Knauf, L. A.; Reisman, D. J.; Peirano, W. B.; DeRosa, C. T.; Gombar, V. K.; Enslein, K.; Carter, J. R.; Blake, B. W.; et al.
CS U.S. Environmental Protection Agency, Cincinnati, OH, USA
SO Toxicology Letters (1995), 79(1-3), 131-43
CODEN: TOLED5; ISSN: 0378-4274
PB Elsevier
DT Journal
LA English
IT **101-61-1**, 4,4'-Methylenebis-(n,n-dimethylaniline) **101-80-4**, 4,4'-Oxydianiline **13552-44-8**, 4,4'-Methylenedianiline dihydrochloride
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(chronic lowest-obsd.-adverse-effect level estn. by QSAR)
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



RN 13552-44-8 CAPLUS
CN Benzenamine, 4,4'-methylenebis-, dihydrochloride (9CI) (CA INDEX NAME)

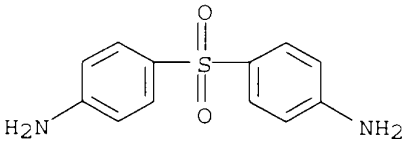


●2 HCl

AB Research was conducted to employ quant. structure-activity relationship (QSAR) techniques to study the feasibility of developing models to est. the noncarcinogenic toxicity of chems. that are not addressed in the literature by relevant studies. A database of lowest-obsd.-adverse-effect level (LOAEL) was assembled by extg. toxicity information from 104 U.S. EPA documents, 124 National **Cancer** Institute/National Toxicol. Program (NCI/NTP) reports, and 6 current reports from the literature. A regression model, based on 234 chems. of diverse structures and chem. classes including both alicyclic and arom. compds., was developed to assess the chronic oral LOAELs in rats. The model was incorporated into an automated computer package. Initial testing of this model indicates it has application to a wide range of chems. For about 55% of the compds. in the data set, the estd. LOAELs are within a factor of 2 of the obsd. LOAELs. For over 93%, they are within a factor of 5. Because of the paucity or absence of long-term toxicity data, the public health and risk assessment community could utilize such QSAR models to det. initial ests. of toxicity for the ever-increasing nos. of chems. that lack complete pertinent data. However, this and other such models should be used only by expert toxicologists who must objectively look at the ests. thus generated in light of the overall wt. of evidence of the available toxicol. information of the subject chem.(s).

L8 ANSWER 42 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1995:678394 CAPLUS
DN 123:104873
TI The procarcinogen hypothesis for bladder **cancer**: Activities of individual drug metabolizing enzymes as risk factors
AU Branch, R. A.; Chern, H. D.; Adedoyin, A.; Romkes-Sparks, M.; Lesnick, T. G.; Persad, R.; Wilkinson, G. R.; Fleming, C. M.; Dickinson, A. J.; et al.
CS Center Clinical Pharmacology, University Pittsburgh, Pittsburgh, PA, 15261, USA
SO Pharmacogenetics (1995), 5(Spec. Issue, ,Spec. Issue), S97-S102
CODEN: PHMCEE; ISSN: 0960-314X
PB Chapman & Hall
DT Journal; General Review

LA English
IT **80-08-0**, Dapsone
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(procarcinogen hypothesis for bladder **cancer**: activities of individual drug metabolizing enzymes as risk factors)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)

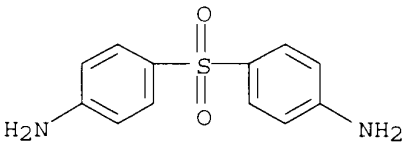


AB Bladder **cancer** provides the most definitive example for an assocn. between environmental agents and **cancer**. However, in the absence of industrial occupational exposure, the primary carcinogen is rarely identified, and the mechanisms involved in **cancer** formation are poorly understood. The environmental procarcinogen hypothesis of tumor pathogenesis proposes that many carcinogens require metabolic activation by drug metabolizing enzymes to form the proximate carcinogen. A balance of exposure to the carcinogen, the activity of the enzymes involved in either formation of proximate carcinogen, or prodn. of non-toxic metabolites, will det. tumor risk. The authors have used mephenytoin, debrisoquine and dapsone as selective probes for the phenotypic measures of activity of CYP2C19, CYP2D6, and CYP3A4, resp. Within subject reproducibility of phenotypic measures, and the lack of cross-inhibition when the three drugs are given in a concurrent cocktail, have been confirmed. The authors have applied the cocktail drug approach in two, non-overlapping series of cases with bladder **cancer** and matched controls. In both series, patients with aggressive bladder **cancer** (GIII histopathol.) had a history of excess alc. intake, an under-representation of poor metabolizers of debrisoquine, a significant mean redn. in dapsone recovery ratio, but no difference in mephenytoin phenotype. Collectively, these observations involving multiple routes of drug metab. support the procarcinogen environmental hypothesis for bladder **cancer** and suggest that measurement of activity of selected individual drug metabolizing enzymes involved in the pathogenesis of this tumor can be used to identify subjects at high risk of developing bladder **cancer**.

L8 ANSWER 43 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1995:459727 CAPLUS
DN 122:212118
TI Use of monoclonal antibodies for determining sensitivity to acetylizable drugs
IN Hammond, Dianne K.
PA Board of Regents, University of Texas System, USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 9504757	A1	19950216	WO 1994-US8882	19940805
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
				US 1993-105439	19930806
	AU 9474520	A1	19950228	AU 1994-74520	19940805
				US 1993-105439	19930806
				WO 1994-US8882	19940805

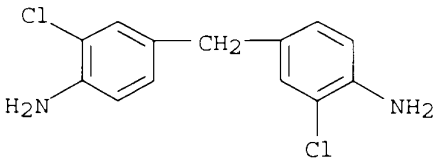
IT **80-08-0**, Dapsone
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal anti-methylxanthine and anti-aminoacetylaminomethyluracil antibodies for detg. sensitivity or risk of toxicity of individual to acetylizable therapeutic drugs)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



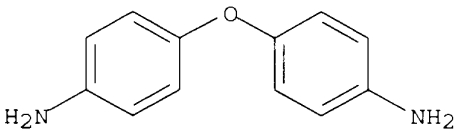
AB Disclosed are monoclonal antibodies having specific binding affinities for 1-methylxanthine (MX) and 5-amino-6-acetylamino-1-methyluracil (AAMU) and hybridoma cell lines producing the monoclonal antibodies. Immunoassay methods for measuring amts. of 5-amino-6-acetylamino-1-methyluracil and 1-methyxanthine in biol. samples are described. An immunoassay method for detn. of an acetylator phenotype of an individual includes detg. a ratio of acetylated metabolite to nonacetylated metabolite in a biol. sample from the individual having been administered an acetylizable drug. The invention also provides an immunoassay method for estg. a likely degree of sensitivity or risk of toxicity to an acetylizable therapeutic drugs, e.g. isoniazid, procainamide, hydralazine, dapsone, sulfamethazine, sulfasalazine, amonafide. In example, MX and AAMU were sep. synthesized, conjugated with hemocyanin or albumin, and used for raising monoclonal antibodies specific to either MX or AAMU. The monoclonal antibodies were used for detg. ratio of acetylated metabolites (MX/AAMU) in urine of individuals administered with caffeine, theophylline or theobromine.

L8 ANSWER 44 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1995:414991 CAPLUS
DN 122:180399
TI Improved prediction of carcinogenic potencies from mutagenic potencies for chemicals positive in rodents and the Ames test
AU Bogen, Kenneth T.
CS Lawrence Livermore Natl. Lab., Univ. California, Livermore, CA, USA
SO Environmental and Molecular Mutagenesis (1995), 25(1), 37-49
CODEN: EMMUEG; ISSN: 0893-6692
PB Wiley-Liss
DT Journal
LA English
IT **101-14-4**, 4,4'-Methylene-bis-2-chloroaniline **101-80-4**, 4,4'-Oxydianiline **139-65-1**, 4,4'-Thiodianiline **13552-44-8**, 4,4'-Methylenedianiline dihydrochloride

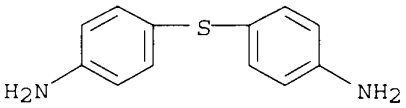
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (prediction of carcinogenic potencies from mutagenic potencies for chems. pos. in rodents and the Ames test)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



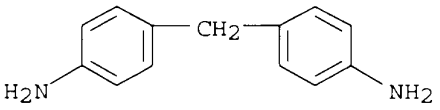
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



RN 13552-44-8 CAPLUS
CN Benzenamine, 4,4'-methylenebis-, dihydrochloride (9CI) (CA INDEX NAME)

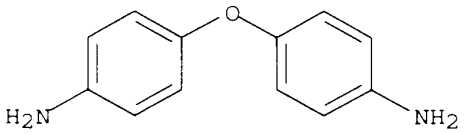


● 2 HCl

AB Most studies of correlation between logs of mutagenic potency (MP) and **cancer** potency (CP) have obtained relatively small but statistically significant ests. of correlation (r) and corresponding log-log slope (b, in Log[CP] = a + b Log[MP]). But for mutagenic carcinogens, multistage **cancer** theory predicts that b and r should be highest when MP values best est. mutation yields per unit dose at concns. at least as high as those obsd. to cause **cancer** in bioassay animals. To test this hypothesis, the correlation of Ames test

and rodent **cancer** potencies was examd. for a total no. n of 134 chems. reported as pos. in both assays. Values of max. significant **cancer** potency (CP, in [mmol/kg-day]-1) were obtained from a published carcinogenic potency data-base. Values of max. mutagenic potency (MP, as revertants per mmol/L-plate) were estd. from 2,347 sets of Ames test data reported by the NTP mutagenicity testing program, supplemented by similar data newly obtained for ten heterocyclic amines. For compds. with one or more significantly pos. MP ests. based on approx. linear Ames test dose-response data, linear regression of max. values of Log(CP) on Log(MP) yielded b = 0.27 and r = 0.39, similar to previously reported results for relatively large n. As predicted, when MP values were addnl. restricted to include only values estd. from Ames test data approx. linear at corresponding lowest-TD50 concns., similar regressions yielded significantly improved fits (e.g., b and r .apprxeq. 0.6, P < 10-7). Implications of these findings are discussed concerning the quant. role that mutations like those measured in the Ames test may have in explaining obsd. **cancer**-bioassay results.

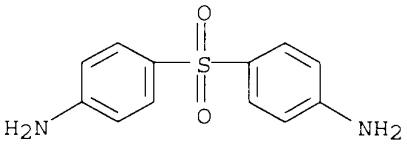
L8 ANSWER 45 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1994:452113 CAPLUS
DN 121:52113
TI Complementarity of genotoxic and nongenotoxic predictors of rodent carcinogenicity
AU Kitchin, Kirk T.; Brown, Janice L.; Kulkarni, Arun P.
CS Health Effects Res. Lab., U.S. Environ. Protect. Agency, Res., Triangle Park, NC, USA
SO Teratogenesis, Carcinogenesis, and Mutagenesis (1994), 14(2), 83-100
CODEN: TCMUD8; ISSN: 0270-3211
DT Journal
LA English
IT **101-80-4**, 4,4'-Oxydianiline
RL: BIOL (Biological study)
(complementarity of genotoxic and nongenotoxic predictors of rodent carcinogenicity in relation to)
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



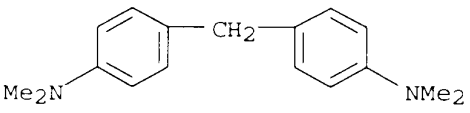
AB Twenty-one chems. carcinogenic in rodent bioassays were selected for study. The chems. were administered by gavage in two dose levels to female Sprague-Dawley rats. The effects of these 21 chems. on four biochem. assays [hepatic DNA damage by alk. elution (DD), hepatic ornithine decarboxylase activity (ODC), serum alanine aminotransferase activity (ALT), and hepatic cytochrome P 450 content (P 450)] were detd. Available data from seven **cancer** predictors published by others [the Ames test (AMES), mutation in Salmonella typhimurium TA 1537 (TA 1537), structural alerts (SA), mutation in mouse lymphoma cells (MOLY), chromosomal aberrations in Chinese hamster ovary cells (ABS), sister chromatid exchange in hamster ovary cells (SCE), and the ke test (ke)] were also compiled for these 21 chem. carcinogens plus 28 carcinogens and 62 noncarcinogens already published by the authors' lab. From the

resulting 111 (chems.) by 11 (individual **cancer** predictors) data matrix, the five operational characteristics (sensitivity, specificity, pos. predictivity, neg. predictivity, and concordance) of each of the 11 individual **cancer** predictors (four biochem. parameters of this study and seven **cancer** predictors of others) are presented. Two examples of complementarity of synergy of composite **cancer** predictors were found. To obtain max. concordance it was necessary to combine both genotoxic and nongenotoxic **cancer** predictors. The composite **cancer** predictor (DD or [ODC and P 450] or [ODC and ALT]) had higher concordance than did any of four individual **cancer** predictors from which it was constructed. Similarly, the composite **cancer** predictor (TA 1537 or DD or [ODC and P 450] or [ODC and ALT]) and higher concordance than any of its five individual constituent **cancer** predictors. Complementarity or synergy has been demonstrated both (1) among genotoxic **cancer** predictors (DD and TA 1537) and (2) between nongenotoxic (ODC, P 450, and ALT) and genotoxic **cancer** predictors (TA 1537 and DD).

L8 ANSWER 46 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1994:402999 CAPLUS
DN 121:2999
TI The relationship between use of the maximum tolerated dose and study sensitivity for detecting rodent carcinogenicity
AU Haseman, Joseph K.; Lockhart, Ann
CS Div. Intramural Res., Natl. Inst. Environ. Health Sci., Research Triangle Park, NC, 27709, USA
SO Fundamental and Applied Toxicology (1994), 22(3), 382-91
CODEN: FAATDF; ISSN: 0272-0590
DT Journal
LA English
IT **80-08-0 101-61-1 101-77-9 101-80-4 139-65-1**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenicity of, in rodents, max. tolerated dose relationship and sensitivity correlation in)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)

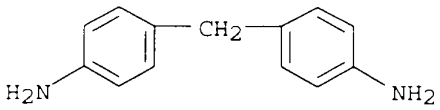


RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)

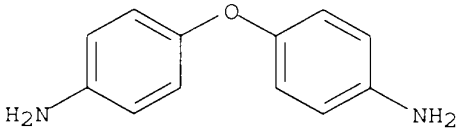


RN 101-77-9 CAPLUS

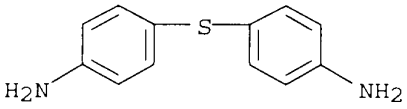
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



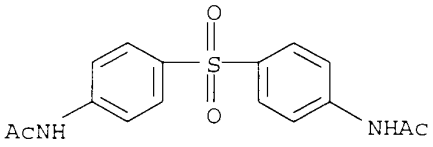
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



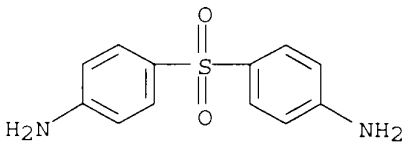
AB The relationship between max. tolerated dose (MTD) and study sensitivity for detecting rodent carcinogenicity was evaluated for 216 chems. found to be carcinogens in lab. animal studies conducted by the National **Cancer** Institute (NCI) and the National Toxicol. Program (NTP). Approx. two-thirds of these rodent carcinogens would have been detected even without the top dose (estd. MTD), but in many of these studies, some site-specific carcinogenic effects would have been missed. Among the remaining one-third of the rodent carcinogens that required the top dose for statistical significance, approx. 80% had numerically elevated rates of the same site-specific tumors at lower doses as well. Only 13 of the NCI/NTP rodent carcinogens had increased tumor rates limited to the top dose for all sites of carcinogenicity. Alternatively, of the 838 site-specific carcinogenic effects obsd. in the NCI/NTP studies, 447 (53%) would have been detected even without the top dose. Of the remaining effects, 75% (294/391) showed numerically elevated site-specific tumor rates at lower doses. The authors' evaluation indicates that most carcinogenic effects obsd. at the top dose in rodent studies are also present (with reduced incidence that might or might not be statistically significant) at the lower doses typically employed (1/2MTD, 1/4MTD).

L8 ANSWER 47 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1993:533233 CAPLUS
DN 119:133233
TI The Influence of chemical structure on the extent and sites of carcinogenesis for 522 rodent carcinogens and 55 different human carcinogen exposures
AU Ashby, J.; Paton, D.
CS Cent. Toxicol. Lab., ICI, Macclesfield/Ches., SK10 4TJ, UK

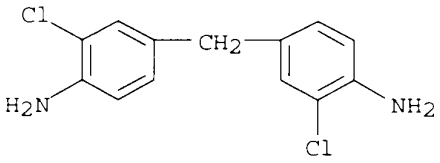
SO Mutation Research (1993), 286(1), 3-74
CODEN: MUREAV; ISSN: 0027-5107
DT Journal
LA English
IT **77-46-3 80-08-0 101-14-4 101-61-1**
101-77-9 101-80-4 139-65-1 838-88-0
17096-29-6, 4,4'-Methylenebis(3-chloroaniline)
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(neoplasm from, of tissues, in lab. animals, structure role in, human in relation to)
RN 77-46-3 CAPLUS
CN Acetamide, N,N'-(sulfonyldi-4,1-phenylene)bis- (9CI) (CA INDEX NAME)



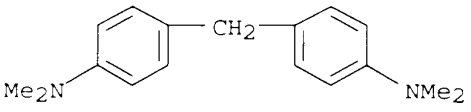
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)

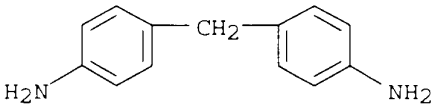


RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)

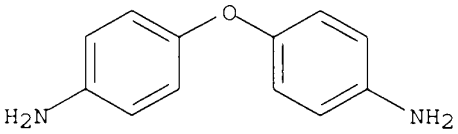


RN 101-77-9 CAPLUS

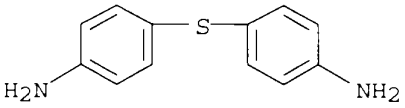
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



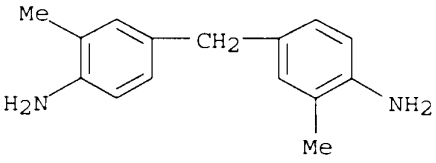
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



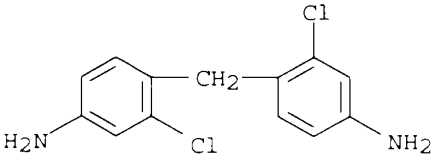
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



RN 838-88-0 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-methyl- (9CI) (CA INDEX NAME)



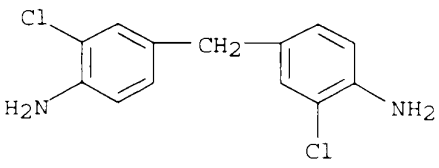
RN 17096-29-6 CAPLUS
CN Benzenamine, 4,4'-methylenebis[3-chloro- (9CI) (CA INDEX NAME)



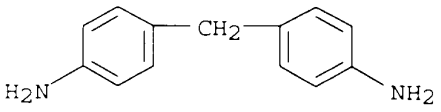
AB L. S. Gold et al. (1991) tabulated the results of rodent bioassays on 522 chems. and analyzed the data. The present study complements those analyses by providing a perspective from the viewpoint of the chem. structure of the carcinogens. The chem. structure of each of the

carcinogens is displayed and the Gold database is represented with the test agents as the primary variable. The carcinogens are gathered into 6 chem. classes and each chem. is assessed for structural alerts to DNA reactivity. The database is then analyzed using an integration of the following parameters: bioassay in rat, mouse or both; structural alert status; chem. class; sites and multiplicity of carcinogenesis, and trans-species carcinogenicity. A series of figures is presented that enables rapid acquaintance with what represents the core database of rodent carcinogenicity. The several analyses presented combine in endorsing the reality of two broad classes of rodent carcinogen, presumed DNA-reactive and others (putative genotoxic and non-genotoxic carcinogens, but semantics have been largely avoided). H. M. Vainio et al. (1991) and his colleagues have tabulated 55 situations in which humans have succumbed to chem. induced **cancer** and have listed the tissues affected. This database of human carcinogens has been analyzed in the present study as done for the rodent carcinogen database, and comparisons made between the two. The predominance of putative genotoxic carcinogens in the human database was confirmed, as was the reality of putative non-genotoxic carcinogenicity in humans. It is concluded that putative genotoxic rodent carcinogenesis can be correlated both with chem. structure and the extent and nature of the induced effect, and that it is of clear relevance to humans. In contrast, it is concluded that putative non-genotoxic rodent carcinogenesis is more closely related to the test species than to the test chem., and that it is essentially unpredictable in the absence of mechanistic models.

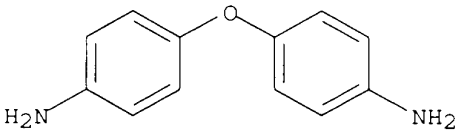
L8 ANSWER 48 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1993:141583 CAPLUS
DN 118:141583
TI Regulation of priority carcinogens and reproductive or developmental toxicants
AU Hooper, Kim; LaDou, Joseph; Rosenbaum, Judith S.; Book, Steven A.
CS California Occup. Health Program, California Dep. Health Serv., Berkeley, CA, 94704, USA
SO American Journal of Industrial Medicine (1992), 22(6), 793-808
CODEN: AJIMD8; ISSN: 0271-3586
DT Journal
LA English
IT **101-14-4**, 4,4'-Methylene bis(2-chloroaniline) **101-77-9** **101-80-4** **139-65-1**, 4,4'-Thiodianiline
RL: PROC (Process)
(as carcinogens, regulation of)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



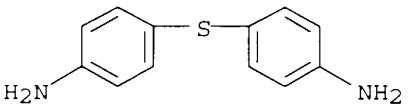
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



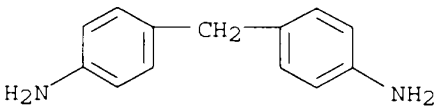
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



AB In California, 370 carcinogens and 112 reproductive/developmental toxicants have been identified as a result of the State's Safe Drinking Water and Toxic Enforcement Act of 1986. They include pesticides, solvents, metals, industrial intermediates, environmental mixts., and reactive agents. Occupational, environmental, and consumer product exposures that involve these agents are regulated under the Act. At levels of concern, businesses must provide warnings for and limit discharges of those chems. The lists of chems. were compiled following systematic review of published data, including tech. reports from the US Public Health Service-National Toxicol. Program (NTP), and evaluation of recommendations from authoritative bodies such as the International Agency for Research on **Cancer** (IARC) and the US Environmental Protection Agency (USEPA). Given the large no. of chems. that are carcinogens or reproductive/developmental toxicants, regulatory concerns should focus on those that have high potential for human exposure, e.g., widely distributed or easily absorbed solvents, metals, environmental mixts., or reactive agents. In this paper, the authors present a list of 33 potential priority carcinogens and reproductive/developmental toxicants, including alc. beverages, asbestos, benzene, chlorinated solvents, formaldehyde, glycol ethers, lead, tobacco smoke, and toluene.

L8 ANSWER 49 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1992:628167 CAPLUS
DN 117:228167
TI Modifying effects of various chemicals on tumor development in a rat wide-spectrum organ carcinogenesis model
AU Uwagawa, Satoshi; Tsuda, Hiroyuki; Ozaki, Keisuke; Takahashi, Satoru; Yamaguchi, Shuji; Mutai, Mamoru; Aoki, Toyohiko; Ito, Nobuyuki
CS Med. Sch., Nagoya City Univ., Nagoya, 467, Japan
SO Japanese Journal of Cancer Research (1992), 83(8), 812-20
CODEN: JJCREP; ISSN: 0910-5050

DT Journal
LA English
IT **101-77-9**, 4,4'-Diaminodiphenylmethane
RL: BIOL (Biological study)
(organ carcinogenesis modification by)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



AB The efficacy of a wide-spectrum organ carcinogenesis model for detection of modification potential of exogenous agents was investigated in F344 male rats. Groups of animals were sequentially injected with N-bis(2-hydroxypropyl)nitrosamine (1000 mg/kg body wt., i.p., in saline, twice in week 1), N-ethyl-N-hydroxyethylnitrosamine (1500 mg/kg body wt., i.g., in distd. water, twice in week 2), and 3,2'-dimethyl-4-aminobiphenyl (75 mg/kg body wt., s.c., in corn oil, twice in week 3) for wide-spectrum initiation of target organs and then given one of 10 test chems., comprising 6 hepatocarcinogens and 4 non-hepatocarcinogens, for 12 wk. All 10 chems. exerted modifying effects in their resp. target organs. An enhancing influence could be detected in the liver and urinary bladder with 2-acetylaminofluorene, ethionine, and 3'-methyl-4-dimethylaminoazobenzene; in the liver and thyroid with 4,4'-diaminodiphenylmethane and phenobarbital; in the esophagus and urinary bladder with N-butyl-N-(4-hydroxybutyl)nitrosamine; in the forestomach and urinary bladder with butylated hydroxyanisole; in the liver with 7,12-dimethylbenz[a]anthracene; and in the liver and lung with 3-methylcholanthrene. Inhibitory effects on development of glutathione S-transferase placental form-pos. liver cell foci were obsd. with clofibrate. The results indicate that the present model can be reliably utilized as a whole body medium-term bioassay system for assessment of environmental **cancer** modifiers.

L8 ANSWER 50 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1992:443667 CAPLUS
DN 117:43667
TI N,N'-(2-aminoethyl)-trans-1,2-diaminocyclohexane-N,N',N'',N'',N''',N'''-hexaacetic acid and related compounds for chelating agents for immunoconjugates
IN Mease, Ronnie C.; Srivastava, Suresh C.; Gestin, Jean Francois
PA Associated Universities, Inc., USA
SO U.S., 13 pp. Cont.-in-part of U.S. 5,021,571.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5089663	A	19920218	US 1991-679258	19910402
				US 1989-372905	19890629
	US 5021571	A	19910604	US 1989-372905	19890629
	US 5334729	A	19940802	US 1991-787244	19911104
				US 1989-372905	19890629

US 1991-679258 19910402

PATENT FAMILY INFORMATION:

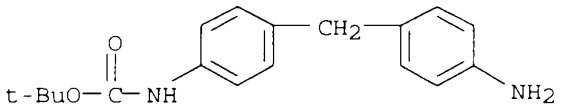
FAN 1992:2915

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5021571	A	19910604	US 1989-372905	19890629
	US 5089663	A	19920218	US 1991-679258	19910402
				US 1989-372905	19890629
	US 5334729	A	19940802	US 1991-787244	19911104
				US 1989-372905	19890629
				US 1991-679258	19910402

IT **135680-03-4P 142247-87-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in cyclohexyl polyaminocarboxylate deriv. prepn. for radiolabeled immunoconjugate prepn.)

RN 135680-03-4 CAPLUS

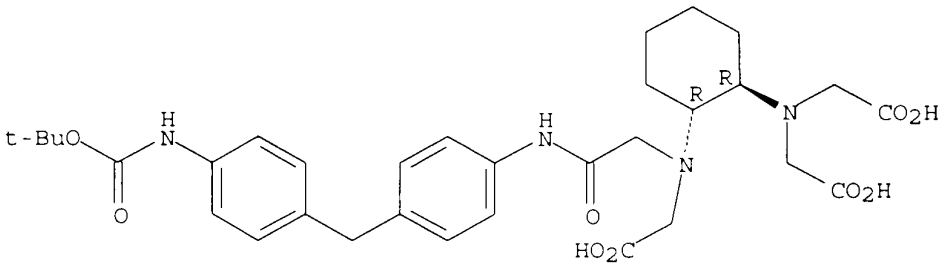
CN Carbamic acid, [4-[(4-aminophenyl)methyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 142247-87-8 CAPLUS

CN Glycine, N-[2-[bis(carboxymethyl)amino]cyclohexyl]-N-[2-[[4-[[4-[[(1,1-dimethylethoxy)carbonyl]amino]phenyl]methyl]phenyl]amino]-2-oxoethyl]-, trans- (9CI) (CA INDEX NAME)

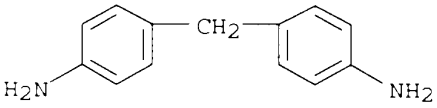
Relative stereochemistry.

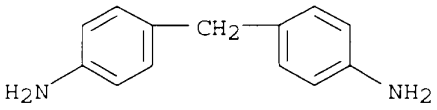


IT **101-77-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in cyclohexyl polyaminocarboxylate deriv. prepn. for radiolabeled immunoconjugate prepn.)

RN 101-77-9 CAPLUS

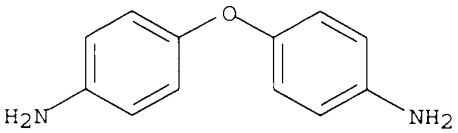
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)





AB Rigid chelating structures are disclosed, as are their prepn. and their use in prepg. radiometal-labeled immunoconjugates. The compds. of the invention include cyclohexyl EDTA monoanhydride, the trans forms of cyclohexyl DTPA and TTHA, and derivs. of these cyclohexyl polyaminocarboxylate materials. The title compd. is specifically claimed. Biodistribution of radiometal-labeled immunoconjugates is included. Cyclohexyl EDTA immunoconjugates (from both monoanhydride and N-hydroxysuccinimide derivs.) with anti-colon **cancer** antibody 17-1A were superior to the nonrigid counterparts with respect to tumor uptake.

L8 ANSWER 51 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1992:249976 CAPLUS
DN 116:249976
TI Predictive assay for rodent carcinogenicity using in vivo biochemical parameters: operational characteristics and complementarity
AU Kitchin, Kirk T.; Brown, Janice L.; Kulkarni, Arun P.
CS Health Effects Res. Lab., U.S. Environ. Protect. Agency, Research Triangle Park, NC, 27711, USA
SO Mutation Research (1992), 266(2), 253-72
CODEN: MUREAV; ISSN: 0027-5107
DT Journal
LA English
IT **101-80-4**, 4,4'-Oxydianiline
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenicity of, predictive assay for, biochem. parameters used in)
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



AB 111 Chems. of known rodent carcinogenicity (49 carcinogens, 62 noncarcinogens), including many promoters of carcinogenesis, nongenotoxic carcinogens, hepatocarcinogens, and halogenated hydrocarbons, were selected for study. The chems. were administered by gavage in two dose levels to female Sprague-Dawley rats. The effects of these 111 chems. on 4 biochem. assays [hepatic DNA damage by alk. elution (DD), hepatic ornithine decarboxylase (ODC) activity, serum alanine aminotransferase (ALT) activity, and hepatic cytochrome P 450 (P 450) content] were detd. Composite parameters are defined as follows: CP = [ODC and P 450), CT = [ALT and ODC), and TS = [DD or CP or CT]. The operational characteristics of TS for predicting rodent **cancer** were sensitivity 55%, specificity 87%, pos. predictivity 77%, neg. predictivity 71%, and concordance 73%. For these chems., the 73% concordance of this study was superior to the concordance obtained from published data from other labs. on the Ames test (53%), structural alerts (SA) (46%), chromosome

aberrations in Chinese hamster ovary cells (48%), cell mutation in mouse lymphoma 15178Y cells (52%), and sister-chromatid exchange in Chinese hamster ovary cells (60%). The 4 in vivo biochem. assays were complementary to each other. The composite parameter TS also shows complementarity to 5 other predictors of rodent **cancer** examd. in this paper. For example, the Ames test alone has a concordance of only 53%. In combination with TS, the concordance is increased to 62% (Ames or TS) or to 63% (Ames and TS). For the 67 chems. with data available for SA, the concordance for predicting rodent carcinogenicity was 47% (for SA alone), 54% (for SA or TS), and 66% (for SA and TS). These biochem. assays will be useful: (1) to predict rodent carcinogenicity per se, (2) to confirm the results of short-term mutagenicity tests by the high specificity mode of the biochem. assays (the specificity and pos. predictivity are both 100%), and (3) to be a component of future complementary batteries of tests for predicting rodent carcinogenicity.

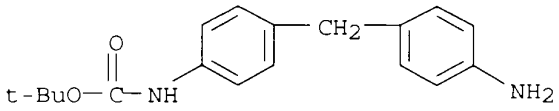
L8 ANSWER 52 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1992:2915 CAPLUS
DN 116:2915
TI Cyclohexyl EDTA monoanhydride for preparation of radiometal-labeled immunoconjugates
IN Mease, Ronnie C.; Srivastava, Suresh C.
PA Associated Universities, Inc., USA
SO U.S., 9 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5021571	A	19910604	US 1989-372905	19890629
	US 5089663	A	19920218	US 1991-679258	19910402
				US 1989-372905	19890629
	US 5334729	A	19940802	US 1991-787244	19911104
				US 1989-372905	19890629
				US 1991-679258	19910402

PATENT FAMILY INFORMATION:
FAN 1992:443667

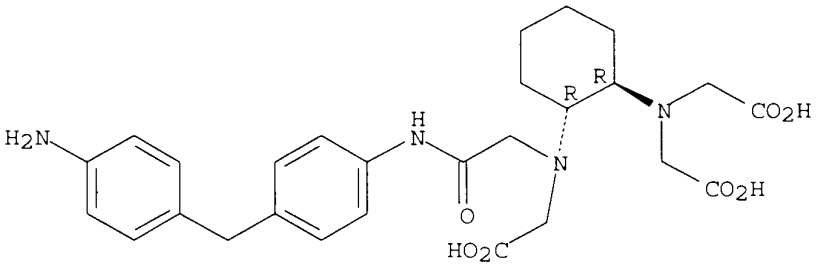
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5089663	A	19920218	US 1991-679258	19910402
				US 1989-372905	19890629
	US 5021571	A	19910604	US 1989-372905	19890629
	US 5334729	A	19940802	US 1991-787244	19911104
				US 1989-372905	19890629
				US 1991-679258	19910402

OS MARPAT 116:2915
IT **135680-03-4P 137731-47-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in immunoconjugate prepn.)
RN 135680-03-4 CAPLUS
CN Carbamic acid, [4-[(4-aminophenyl)methyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



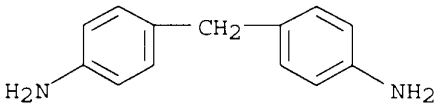
RN 137731-47-6 CAPLUS
CN Glycine, N-[2-[[4-[(4-aminophenyl)methyl]phenyl]amino]-2-oxoethyl]-N-[2-[bis(carboxymethyl)amino]cyclohexyl]-, monohydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

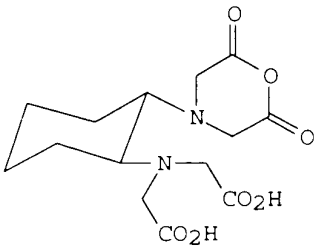


● HCl

IT **101-77-9**, 4,4'-Methylenedianiline
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in immunoconjugate prepn.)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



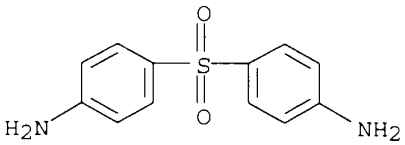
GI



I

AB Title compd. I is claimed. I, and the family of new compds. produced by the derivatization of I, are prepd. and conjugated to monoclonal antibodies predominantly through lysine groups on the antibody without crosslinking of the antibody. The immunoconjugate formed using the chelating agent produce stable complexes with many radiometals. Many of these complexes are more stable in serum than those formed using non-rigid chelates such as EDTA and DTPA. 111In-labeled CDTA, trans-CDTPA, and trans-CTTHA (CDTPA = cyclohexyl DTPA; CTTHA = cyclohexyl TTHA; prepns. given) conjugates with anticolon carcinoma monoclonal antibody 17-1A as well as their nonrigid counterparts EDTA, DTPA, and TTHA were tested in human colon **cancer** (SW948) xenografted nude mice. The tumor uptake of CDTA and trans-CTTHA conjugates was 3-4 times higher than EDTA and TTHA conjugates. They also had slower whole body and blood clearance as well as decreased kidney excretion.

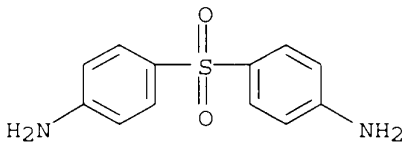
L8 ANSWER 53 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1992:2068 CAPLUS
DN 116:2068
TI Quantitative prediction of human **cancer** risk from rodent carcinogenic potencies: a closer look at the epidemiological evidences for some chemicals not definitively carcinogenic in humans
AU Goodman, Gay; Wilson, Richard
CS Dep. Phys., Harvard Univ., Cambridge, MA, 02138, USA
SO Regulatory Toxicology and Pharmacology (1991), 14(2), 118-46
CODEN: RTOPDW; ISSN: 0273-2300
DT Journal
LA English
IT **80-08-0**, Dapsone
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenicity of, in rodents, human **cancer** risk assessment from)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



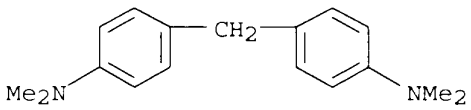
AB The authors performed quant. comparisons of the rodent and human carcinogenic potencies in these same chems. Starting with the rodent TD50 at the most sensitive site, the authors derived a predicted human incidence for the degree of exposure and duration of follow-up corresponding to the most comprehensive epidemiol. study available, and then compared the predicted incidence with the obsd. incidence. If a chem. produced no statistically significant increase in **cancer** at any site in the exposed population, consistency with rodent results is inferred if the min. rodent TD50 is sufficiently high that no attributable cases would have been expected under the actual conditions of human exposure and follow-up. For 18 of the 22 chems. examd., the human evidence is consistent with the predictions based on the rodent bioassay results. For 2 chems., dichlorobenzidine and ethylene thiourea, there is not enough epidemiol. information to make a useful comparison with rodent bioassay data. For the 2 remaining chems., actinomycin D and vinylidene

chloride, the human evidence is inconsistent with the predictions. But the conditions of the rodent bioassay of actinomycin D were inappropriate for the comparison, and for vinylidene chloride the human exposure dose and duration were uncertain; either chem. might yet demonstrate consistency with the rodent results in future epidemiol. studies.

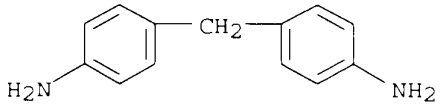
L8 ANSWER 54 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1991:600827 CAPLUS
DN 115:200827
TI Definitive relationships among chemical structure, carcinogenicity and mutagenicity for 301 chemicals tested by the U.S. NTP
AU Ashby, John; Tennant, Raymond W.
CS Cent. Toxicol. Lab., ICI, Cheshire, SK10 4TJ, UK
SO Mutation Research (1991), 257(3), 229-306
CODEN: MUREAV; ISSN: 0027-5107
DT Journal
LA English
IT **80-08-0**, 4,4'-Sulfonyldianiline **101-61-1**
101-77-9 101-80-4 139-65-1, 4,4'-Thiodianiline
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(carcinogenic and mutagenic anal. of, structure in relation to)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



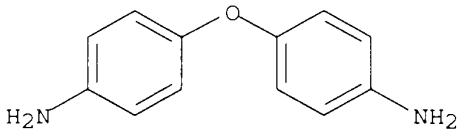
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



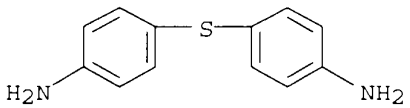
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



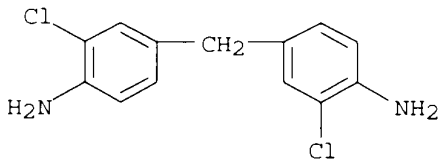
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



AB An anal. is presented in which correlations among chem. structure, mutagenicity to Salmonella, and carcinogenicity to rats and mice among 301 chems. tested by the U.S. NTP are evaluated. Overall, there was a high correlation between structural alerts to DNA reactivity and mutagenicity, but the correlation of either property with carcinogenicity was low. If rodent carcinogenicity is regarded as a singular property of chems., then neither structural alerts nor mutagenicity to Salmonella are effective in its prediction. Given this, the database was fragmented and new correlations sought between the derived subgroups. First, the 301 chems. were segregated into six broad chem. groupings. Second, the rodent **cancer** data were partially segregated by target tissue. Using the previously assigned structural alerts to DNA reactivity (electrophilicity), the chems. were split into 154 alerting chems. and 147 nonalerting chems. The alerting chems. were split into three chem. groups: arom. amino/nitro-types, alkylating agents, and misc. structurally alerting groups. The nonalerting chems. were subjectively split into three broad categories: nonalerting, nonalerting contg. a nonreactive halogen group, and nonalerting chems. with minor concerns about a possible structural alert. The tumor data for all 301 chems. are represented according to these six chem. groupings. The most significant findings to emerge from comparisons among these six groups of chems. were as follows: most of the rodent carcinogens, including most of the 2-species and/or multiple site carcinogens, were among the structurally alerting chems. Most of the structurally alerting chems. were mutagenic: 84% of the carcinogens and 66% of the noncarcinogens. Some 100% of the 33 arom. amino/nitro-type 2-species carcinogens were mutagenic. Thus, for structurally alerting chems., the Salmonella assay showed high sensitivity and low specificity (0.84 and 0.33, resp.). Among the 147 nonalerting chems., <5% were mutagenic, whether they were carcinogens or noncarcinogens (sensitivity 0.04).

L8 ANSWER 55 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1991:234266 CAPLUS
DN 114:234266
TI Biological monitoring of a worker acutely exposed to MBOCA
AU Osorio, Ana Maria; Clapp, David; Ward, Elizabeth; Wilson, H. Kerr; Cocker, John
CS DSHEFS, NIOSH, Cincinnati, OH, USA
SO American Journal of Industrial Medicine (1990), 18(5), 577-89
CODEN: AJIMD8; ISSN: 0271-3586
DT Journal

LA English
IT **101-14-4**, MBOCA
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(occupational exposure to, in plastic products manuf., biol. monitoring of worker in relation to)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



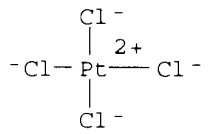
AB A 30 yr-old male polyurethane worker was exposed to an accidental spill of 4,4'-methylene-bis-2-chloroaniline (MBOCA) at a plant producing MBOCA-cured plastic products. The employee was sprayed over his upper body and extremities with molten MBOCA while cleaning out a clogged hose from a MBOCA and polymer mixing machine. The subsequent environmental and medical evaluation of this episode included serial urinary MBOCA samples from the worker over a 2 wk period to allow the calcn. of a biol. half-life for this compd. This worker experienced a very high dose of MBOCA as judged by his urinary MBOCA levels (peak value of 1700) ppb 4 h after exposure). There were no acute symptoms or other lab. abnormalities noted. The kinetic evaluation resulted in a biol. half-life for MBOCA in urine of approx. 23 h. Assuming a one-compartment model, approx. 94% of an initial MBOCA dose will be eliminated within four days. This is the first report of kinetic anal. on urinary MBOCA excretion in humans. This information suggests that biol. monitoring of the urine MBOCA concns. in exposed workers may miss peak levels following an acute exposure unless the analyses of the urinary MBOCA are performed in a timely fashion. Recommendations to the company included: (1) installation of a warning system or lock-out device on the mixing machine to prevent the opening of the MBOCA hose prior to the release of pressure; and (2) annual medical surveillance of this individual for bladder **cancer** with urinalysis and urine cytol.

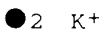
L8 ANSWER 56 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1991:220758 CAPLUS
DN 114:220758
TI Platinum(II) polyamines: relationship of chain length to biological activity
AU Siegmann, Deborah W.; Carraher, Charles E., Jr.; Brenner, Dora
CS Dep. Chem., Florida Atlantic Univ., Boca Raton, FL, 33431, USA
SO Prog. Biomed. Polym., [Proc. Am. Chem. Soc. Symp.] (1990), Meeting Date 1988, 371-88. Editor(s): Gebelein, Charles G.; Dunn, Richard L. Publisher: Plenum, New York, N. Y.
CODEN: 57BPAS
DT Conference
LA English
IT **126250-01-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm inhibiting activity of, chain length effect on)

RN 126250-01-9 CAPLUS
CN Platinate(2-), tetrachloro-, (SP-4-1)-, dipotassium, polymer with 4,4'-sulfonylbis[benzenamine] (9CI) (CA INDEX NAME)

CM 1

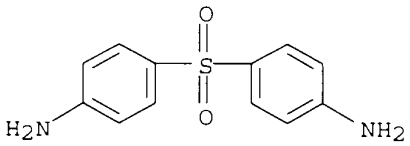
CRN 10025-99-7
CMF Cl4 Pt . 2 K
CCI CCS





CM 2

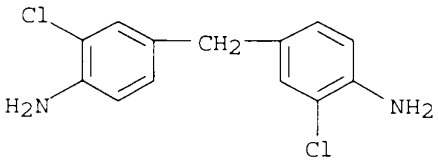
CRN 80-08-0
CMF C12 H12 N2 O2 S



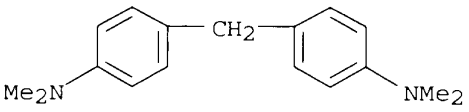
AB Platinum (II) polyamines, which are polymeric analogs of the **cancer** drug cis-DDP, were synthesized and tested for biol. activity. The results obtained from cell culture show that several of the polymers kill cells and/or inhibit cell growth of growing cells but do not affect quiescent cells. The level of activity displayed by these polymers is equal to or greater than that of cis-DDP. Since some polymers are biol. active, while others are not, several factors which could influence activity were considered. The polymer chain length could det. how easily the polymer enters the cell and how well it binds to and damages cellular macromols. The size of the various platinum polyamines was measured by using light scattering photometry and Sephacryl column chromatog. No correlation was seen between the size of a polymer and its biol. activity. Mol. wt. does not appear to be an important factor in detg. the biol. effects of these platinum polyamines.

L8 ANSWER 57 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1991:180094 CAPLUS
DN 114:180094
TI Regulation of occupational carcinogens under OSHA's air contaminants standard
AU Paxman, Dalton G.; Robinson, James C.

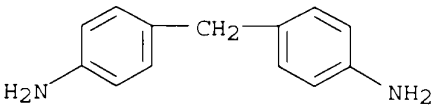
CS Sch. Public Health, Univ. California, Berkeley, CA, 94720, USA
SO Regulatory Toxicology and Pharmacology (1990), 12(3, Pt. 1), 296-308
CODEN: RTOPDW; ISSN: 0273-2300
DT Journal
LA English
IT **101-14-4 101-61-1 101-77-9**
RL: BIOL (Biological study)
(carcinogenic activity of, evaluation of, occupational carcinogen regulation under air contaminants std. in relation to)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



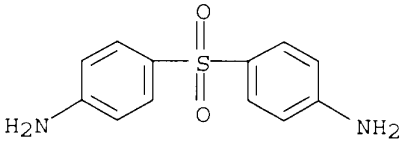
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



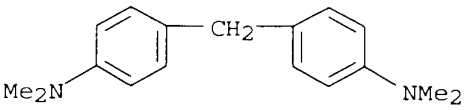
AB The information used by the Occupational Safety and Health Administration (OSHA) to regulate carcinogens under its 1989 Air Contaminants Std. to publicly available information on substances with potential carcinogenic activity was compared. Carcinogenicity evaluations were obtained from the National Institute for Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), the National Toxicol. Program (NTP), the Environmental Protection Agency (EPA), and the International Agency for Research on **Cancer** (IARC). Three sets of substances were analyzed: those which were regulated as carcinogens by OSHA in the std., those which were included in the std. but whose exposure limits are based on noncarcinogenic effects, and those substances designated as potential carcinogens by NIOSH, ACGIH, and/or NTP but which were excluded from the std. The data indicate that OSHA relied almost exclusively upon the recommendations of the nongovernmental ACGIH to the exclusion of IARC and the three governmental bodies. Given their statutory authority to evaluate chem. carcinogenicity for regulatory agencies such as OSHA, the exclusion of NIOSH and NTP is

particularly striking.

L8 ANSWER 58 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1991:19021 CAPLUS
DN 114:19021
TI Response of the ke test to NCI/NTP-screened chemicals. I. Nongenotoxic carcinogens and genotoxic non-carcinogens
AU Bakale, George; McCreary, Richard D.
CS Radiol. Dep., Case West. Reserve Univ., Cleveland, OH, 44106, USA
SO Carcinogenesis (1990), 11(10), 1811-18
CODEN: CRNGDP; ISSN: 0143-3334
DT Journal
LA English
IT **80-08-0**, Dapsone **101-61-1**
RL: PRP (Properties)
(electrophilicity of, genotoxic noncarcinogens and nongenotoxic carcinogens in relation to)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



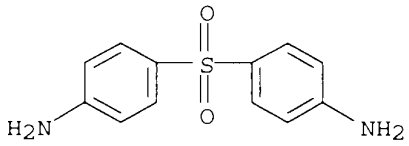
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



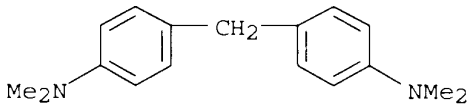
AB The responses of a physicochem. carcinogen-screening test, the ke test, to 46 rodent carcinogens and 20 putative noncarcinogens that had been screened in long-term two-species bioassays by the National **Cancer** Institute/National Toxicol. Program are reported. All of the chems. screened are those that yield mutagenicity responses in the Ames Salmonella/microsome test that are either equivocal or contrary to the rodent carcinogenicity responses. The electron attachment rate consts., kes, of the test chems. in cyclohexane at 21.degree. were measured using a pulse-cond. technique. The kes of 27 of the 46 rodent carcinogens (59%) are equal or greater than the diffusion-controlled ke of carbon tetrachloride, which is regarded as the boundary between a pos. and neg. response; the kes of 8 of the 20 mutagenic noncarcinogens (40%) are less than diffusion-controlled. If the boundary between pos. and neg. ke responses is decreased to half the diffusion-controlled ke, six addnl. carcinogens yield a pos. ke response which increases the ke test sensitivity to 72% whereas the specificity to noncarcinogens remains at 40%. Comparison of these kes with measures of the chems.' electrophilicity that had been inferred from chem. structure indicates that ke provides a markedly different measure of electrophilicity and one

that complements the Ames Salmonella assay. The use of the ke test as an anal. tool to indicate the presence of electron-attaching impurities in solvents such as benzene is discussed, as is the sensitivity of the ke test to rodent liver carcinogens.

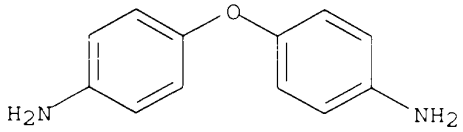
L8 ANSWER 59 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1991:2044 CAPLUS
DN 114:2044
TI ICPEMC working paper 1/2: a multi-factor ranking scheme for comparing the carcinogenic activity of chemicals
AU Nesnow, Stephen
CS Carcinog. Metab. Branch, U. S. Environ. Prot. Agency, Research Triangle Park, NC, 27711, USA
SO Mutation Research (1990), 239(2), 83-115
CODEN: MUREAV; ISSN: 0027-5107
DT Journal
LA English
IT **80-08-0**, Dapsone **101-61-1**, 4,4'-Methylene bis(N,N-dimethylaniline) **101-80-4**, 4,4'-Oxydianiline **139-65-1**, 4,4'-Thiodianiline
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenicity of, ranking scheme for)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



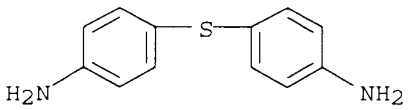
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



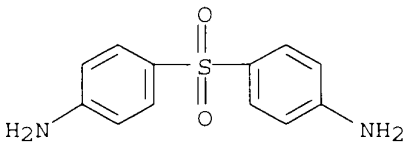
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



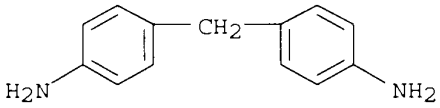
AB A scheme for ranking the quant. activity of chem. carcinogens is described. This activity scheme uses as its base, dose potency measured as median tumorigenic dose TD50, the chronic dose rate that actuarially halves the adjusted percentage of tumor-free animals at the end of the study (L.S. Gold et al., 1986). The TD50 is converted into an inverse log scale, a decile scale, and then adjusted by weighting factors that describe other parameters of carcinogenic activity. These factors include pos. or neg. weightings for: the induction of tumors at tissues or organs assocd. with high historical control tumor incidences; the induction of tumors at multiple sites; the induction of tumors in both sexes of the species; and the induction of tumors in more than one species. These factors were chosen as they represented qual. descriptions of the general specificity or nonspecificity of chems. with regard to the activity in rodents and have some bearing on the potential activity of chems. in humans. In order to construct a measure to express the inactivity of chems. towards the induction of **cancer**, a measure analogous to the TD50 has been developed: the highest av. daily dose (HADD). The HADD is the highest av. daily dose in mg chem./kg administered in a chronic **cancer** study and that did not induce a statistical increase in tumors. HADD values were similarly converted to log decile units and adjusted by weighting factors according to lack of activity in both sexes of a species, and the lack of activity in more than one species. In order to explore the use of this multifactor activity scheme for both carcinogens and noncarcinogens, a group of 142 chems. was selected that had been tested according to an oral dosing protocol in two sexes of two species of rodents and whose data was peer-reviewed and available for this anal. This data came from the National Toxicol. Program/National **Cancer** Institute Bioassay Tech. Reports. Three activity ranking schemes were developed: the Carcinogen Activity-F344 Rat, an activity scheme based on **cancer** data obtained with the F344 rat; the Carcinogen Activity-B6C3F1 Mouse, an activity scheme based on **cancer** data obtained with the B6CF1 mouse, and the Carcinogen Activity-Combined, and activity scheme based on selecting data from both the F344 rat and the B6C3F1 mouse. This selection was based on the most sensitive rodent responding to the carcinogenic activity of active chems. and the least sensitive rodent responding to the toxic effects of inactive chems. This paper discusses the construction and development of these ranking schemes and analyzes the results in terms of distributions of values within each ranking scheme, and the relative contributions of TD50 (or HADD) and the weighting factor in the activity schemes.

L8 ANSWER 60 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1990:493117 CAPLUS
DN 113:93117
TI Rodent tumor profiles, Salmonella mutagenicity and risk assessment
AU Benigni, R.
CS Lab. Tossicol. Comp. Ecotossicol., Ist. Super. Sanita, Rome, I-00161, Italy
SO Mutation Research (1990), 244(1), 79-91
CODEN: MUREAV; ISSN: 0027-5107
DT Journal

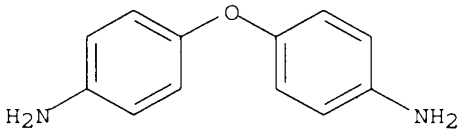
LA English
IT **80-08-0**, 4,4'-Sulfonyldianiline **101-77-9**,
4,4'-Methylenedianiline **101-80-4 139-65-1**,
4,4'-Thiodianiline
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenicity and mutagenicity of, classification in relation to)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



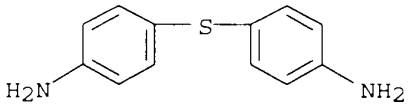
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



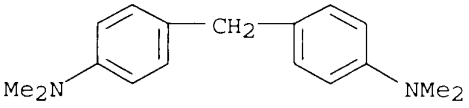
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



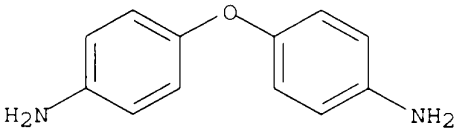
AB The tumorigenesis profiles of 116 chems., which proved to induce **cancer** in the NCI/NTP experimentation, were studied by multivariate data anal. methods. Three main patterns of tumor induction were evident. One chem. (benzene) was not classifiable in any of the 3 clusters of chems. The carcinogen classes based on patterns of tumor induction did not reflect a repartition between Ames-pos. and Ames-neg. chems. Therefore any classification of carcinogens as either primary (genotoxic, hence assumed to pose a greater risk) or secondary (presumably carcinogenic via nongenotoxic mechanisms) would seem to be a subject for

research and speculation, and, for the present, an unsuitable basis for risk assessment.

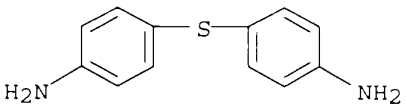
L8 ANSWER 61 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1990:472856 CAPLUS
DN 113:72856
TI Prediction of **cancer** potency using a battery of mutation and toxicity data
AU Travis, C. C.; Saulsbury, A. W.; Pack, S. A. Richter
CS Health Saf. Res. Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37831-6109, USA
SO Mutagenesis (1990), 5(3), 213-19
CODEN: MUTAEX; ISSN: 0267-8357
DT Journal
LA English
IT **101-61-1 101-80-4 139-65-1**
RL: PRP (Properties)
(carcinogenic potential of, from mutation and toxicity data battery)
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



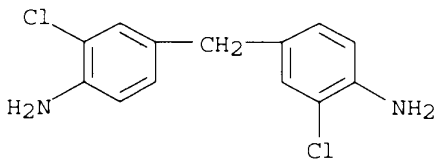
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



AB Correlations between the carcinogenic potencies of 146 known mouse carcinogens and potency ests. detd. from (i) Ames test results, (ii) a battery of mutation test results, and (iii) a battery of mutation and toxicity data are presented. The lowest correlation was found using Salmonella mutagenic potency (r = 0.37). The highest correlations were found using the battery of mutation and toxicity data to predict the potency of lung carcinogens (r = 0.94) and liver carcinogens (r = 0.91). The results suggest that short-term batteries which include tests for mutagenicity and toxicity will be able to predict carcinogenic potency

better than current batteries relying solely on mutagenicity tests.

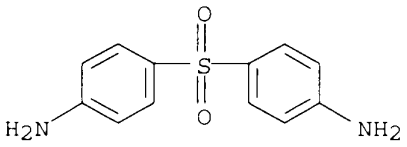
L8 ANSWER 62 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1990:134245 CAPLUS
DN 112:134245
TI 4,4'-Methylene-bis(2-chloroaniline) (MOCA): comparison of macromolecular adduct formation after oral or dermal administration in the rat
AU Cheever, Kenneth L.; Richards, Donald E.; Weigel, Walter W.; Begley, Karen B.; DeBord, D. Gayle; Swearengin, Terri F.; Savage, Russell E., Jr.
CS Dep. Health Hum. Serv., Natl. Inst. Occup. Saf. and Health, Cincinnati, OH, 45226, USA
SO Fundamental and Applied Toxicology (1990), 14(2), 273-83
CODEN: FAATDF; ISSN: 0272-0590
DT Journal
LA English
IT **101-14-4D**, 4,4'-Methylene-bis(2-chloroaniline), reaction products with Hb and DNA
RL: FORM (Formation, nonpreparative)
(formation of)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



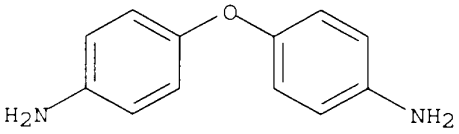
AB The macromol. binding of MOCA, a suspect human carcinogen, was studied in the adult male Sprague-Dawley rat after both oral and dermal administration. Rats were euthanized 1-29 days after a single 281 .mu.mol/kg dose of [14C]MOCA (oral, 213 .mu.Ci/kg; dermal, 904 .mu.Ci/kg). DNA from various tissues and Hb were isolated for detn. of the time course of MOCA macromol. binding. After oral administration adduct formation was rapid with max. levels appearing at 24 h. The 24-h covalent binding assocd. with the globin was 7.84 pmol/mg globin (t1/2 = 14.3 days). More extensive 24-h covalent binding was detected for liver DNA with 49.11 pmol-mg DNA (t1/2 = 11.1 days). After dermal administration of MOCA the major portion of the dose, 86.2%, remained at the application site throughout the study. For these rats the 24-h covalent binding detd. for liver DNA was 0.38 pmol/mg DNA (t1/2 = 15.6 days). Although lower levels were detected after dermal application, similar stability of MOCA-DNA adducts indicates that quantification of such MOCA adducts may be useful for the long-term industrial biomonitoring of MOCA exposure and for the evaluation of human DNA-MOCA adduct formation, a lesion thought to be assocd. with the prodn. of **cancer**.

L8 ANSWER 63 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1989:589324 CAPLUS
DN 111:189324
TI Combination effects of forty carcinogens administered at low doses to male rats
AU Takayama, Shozo; Hasegawa, Hirokazu; Ohgaki, Hiroko
CS Res. Inst., Natl. Cancer Cent., Tokyo, 104, Japan
SO Japanese Journal of Cancer Research (1989), 80(8), 732-6

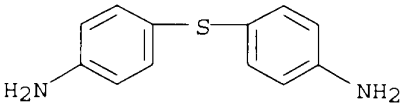
CODEN: JJCREP; ISSN: 0910-5050
DT Journal
LA English
IT **80-08-0**, Dapsone **101-80-4**, 4,4'-Diaminodiphenyl ether
139-65-1, 4,4'-Thiodianiline
RL: BIOL (Biological study)
(carcinogenicity of mixts. contg.)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



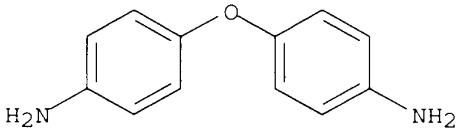
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



AB An investigation was conducted to det. whether a mixt. of low doses of forty carcinogens that target different organs, including the liver, intestine, thyroid, urinary bladder, and skin, is effective for tumor induction in F344/DuCrj rats. The dose of each carcinogen in the diet was 1/50 of the TD50 value, treatment being continued for 102 wk. Significant nos. of neoplastic nodules of the liver and follicular cell tumors of the thyroid developed in the animals exposed to the carcinogen mixt., although the question of whether the obsd. carcinogenic effects were synergistic or additive could not be answered. The results serve to evaluate carcinogenic risk in the search for causes of human **cancer**.

L8 ANSWER 64 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1989:419169 CAPLUS
DN 111:19169
TI Preliminary estimates of the virtually safe dose for tumors obtained from the maximum tolerated dose
AU Gaylor, David W.
CS Natl. Cent. Toxicol. Res., U.S. Food Drug Adm., Jefferson, AR, 72079, USA

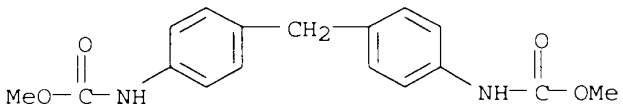
SO Regulatory Toxicology and Pharmacology (1989), 9(2), 101-8
CODEN: RTOPDW; ISSN: 0273-2300
DT Journal
LA English
IT **101-80-4**, 4,4'-Oxydianiline
RL: BIOL (Biological study)
(max. tolerated dose and virtually safe dose of, correlation of, in humans and lab. animals)
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



AB The correlation was studied between the max. tolerated dose (MTD) and the low-dose est. of the virtually safe dose (VSD) for animal carcinogens. Chronic bioassay results from the National **Cancer** Institute/National Toxicol. Program carcinogenesis screening program were used. Ests. of the VSD were obtained by linear low-dose extrapolation for which an adequate dose-response relationship existed at the same tumor site in the same sex for both rats and mice. Ests. of the VSD were compared with the MTD for 69 tumor sites from 38 chems. for rats and mice. The MTDs ranged from high to low toxicity (1 ppb to 4.4% in the diet). The overall geometric mean of the ratio of the MTD to the VSD corresponding to a max. estd. risk of 10-6 was 3.8 .times. 105. Of the 138 cases, only 3 cases were more than a factor of 10 from the mean ratio. This suggested that a quick est. of the VSD could be obtained by dividing the MTD, obtained from a subchronic study, by 400,000. Further, if the human exposure is less than 10-7 .times. MTD, the estd. risk is likely to be negligible even if the chem. is a carcinogen. It may not be worthwhile to conduct a chronic bioassay for the purpose of demonstrating a negligible risk, if the chem. is likely to be carcinogenic, unless the human exposure is extremely low. For example, if the human exposure is greater than 10-3 .times. MTD, the upper limit on the estd. risk is likely to exceed 10-5, if the chem. is carcinogenic in the bioassay.

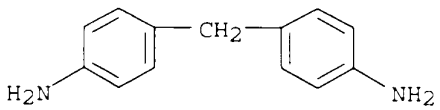
L8 ANSWER 65 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1989:205064 CAPLUS
DN 110:205064
TI Tubulin-dependent hydrolysis of guanosine triphosphate as a screening test to identify new antitubulin compounds with potential as antimitotic agents: application to carbamates of aromatic amines
AU Chi, Duanmu; Shahrik, Lilian K.; Ho, Holly H.; Hamel, Ernest
CS Lab. Biochem. Pharmacol., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SO Cancer Research (1989), 49(6), 1344-8
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
IT **7450-63-7**, NSC 215914
RL: BIOL (Biological study)
(antimitotic activity of, neoplasm inhibition from, structure in relation to)
RN 7450-63-7 CAPLUS

CN Carbamic acid, (methylenedi-4,1-phenylene)bis-, dimethyl ester (9CI) (CA INDEX NAME)



AB Tubulin-dependent GTP hydrolysis was evaluated for its potential as a relatively simple screening assay for new antimitotic drugs. Carbamates of arom. amines were chosen as the test system because of the relatively diverse structures of compds. in this class already known to have antimitotic properties and because of the large no. of such compds. in the NSC collection of the National **Cancer** Institute. Of 162 compds. evaluated, alterations in the GTPase reaction were obsd. with 26 agents. Sixteen of these had substantial inhibitory effects on tubulin polymn. (true positives), while 10 did not (false positives). There were no false negatives (i.e., no agent inactive in the GTPase assay inhibited tubulin polymn.). The true positives were examd. for effects on cell growth and mitosis, and 4 compds. had 50% inhibitory concn. values of .ltoreq.2 .mu.M with L1210- murine leukemia cells. All 4 caused the accumulation of cells in metaphase arrest. Thus, tubulin-dependent GTP hydrolysis can be used effectively to select new antitubulin compds. with potential as antimitotic agents from a large group of compds. of unknown activity.

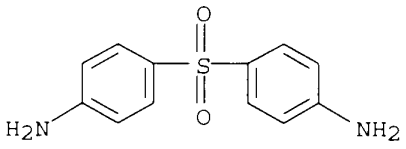
L8 ANSWER 66 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1988:466216 CAPLUS
DN 109:66216
TI Validity of short-term examination for antipromoters of bladder carcinogenesis
AU Kakizoe, Tadao; Takai, Kazuhiro; Tobisu, Kenichi; Ohtani, Mikinobu; Sato, Shigeaki
CS Urol. Div., Natl. Cancer Cent. Hosp., Tokyo, 104, Japan
SO Japanese Journal of Cancer Research (1988), 79(2), 231-5
CODEN: JJCREP; ISSN: 0910-5050
DT Journal
LA English
IT **101-77-9**, p,p'-Diaminodiphenylmethane
RL: PRP (Properties)
(antipromoter effects of, on bladder carcinogenesis)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



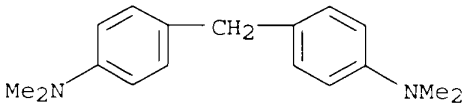
AB Various compds. were screened for antipromoter activity in bladder carcinogenesis in rats with a view to using them clin. to inhibit postoperative intravesical ectopic tumor growth of superficial papillary bladder **cancer**. Their inhibitions of the effect of Na saccharin in maintaining increased agglutinability of bladder cells by Con A were examd. in 4-wk tests. The compds. found to inhibit the effect of

saccharin were .alpha.-tocopherol, ascorbic acid, aspirin, all-trans arom. retinoid, .alpha.-difluoromethylornithine, sodium cyanate and p,p'-diaminodiphenylmethane. Considering the toxicities of some of these chems., ascorbic acid and .alpha.-difluoromethylornithine were concluded to be the most promising for future clin. trials.

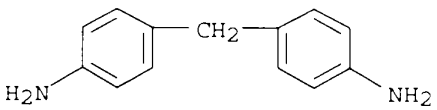
L8 ANSWER 67 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1988:163022 CAPLUS
DN 108:163022
TI Chemical structure, Salmonella mutagenicity and extent of carcinogenicity as indicators of genotoxic carcinogenesis among 222 chemicals tested in rodents by the U.S. NCI/NTP
AU Ashby, John; Tennant, Raymond W.
CS Cent. Toxicol. Lab., ICI PLC, Macclesfield/Cheshire, UK
SO Mutation Research (1988), 204(1), 17-115
CODEN: MUREAV; ISSN: 0027-5107
DT Journal
LA English
IT **80-08-0**, 4,4'-Sulfonyldianiline **101-61-1**
101-77-9, 4,4'-Methylenedianiline **101-80-4**,
4,4'-Oxydianiline **139-65-1**, 4,4'-Thiodianiline
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(carcinogenicity and mutagenicity of, structure in relation to)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



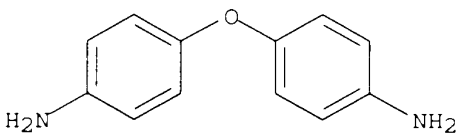
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



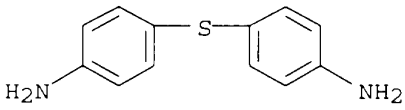
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



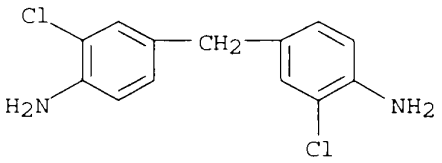
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



AB A survey was conducted of 222 chems. evaluated for carcinogenicity in mice and rats by the US NCI/NTP. The structure of each chem. was assessed for potential electrophilic (DNA-reactive) sites, its mutagenicity to Salmonella recorded, and the level of its carcinogenicity to rodents tabulated. Correlations among these 3 parameters were then sought. A strong assocn. exists among chem. structure (S/A), mutagenicity to Salmonella, and the extent and sites of rodent tumorigenicity among the 222 compds. Thus, an .apprx.90% correlation exists between S/A and mutagenicity across the 115 carcinogens, the 24 equivocal carcinogens, and the 83 noncarcinogens. This indicates that the Salmonella is a sensitive method of detecting intrinsic genotoxicity in a chem. Concordance between S/A and mutagenicity have therefore been employed as an index of genotoxicity, and use of this index reveals 2 groups of carcinogens within the data base, genotoxic and putatively nongenotoxic. These 2 broad groups are characterized by different overall carcinogenicity profiles. Thus, 16 tissues were subject to carcinogenesis only by genotoxins, chief among which were the stomach, Zymbal's glands, lung, s.c. tissue, and the circulatory system. Conclusions of carcinogenicity in these 16 tissues comprised 31% of the individual chem./tissue reports of carcinogenicity. In contrast, both genotoxins and nongenotoxins were active in the remaining 13 tissues, chief among which was the mouse liver which accounted for 24% of all chem./tissue reports of carcinogenicity. Further, the group of 70 carcinogens reported to be active in both species and(or) in 2 or more tissues contained a higher proportion of Salmonella mutagens (70%) than obsd. for the group of 45 single-species/single-tissue carcinogens (39%). 30% Of the 83 noncarcinogens were mutagenic to Salmonella. This confirms earlier observations that a significant proportion of in vitro genotoxins are noncarcinogenic, probably due to their nonabsorption or preferential detoxification in vivo. Also, only 30% of the mouse liver-specific carcinogens were mutagenic to Salmonella. This is consistent with tumors being induced in this tissue (and to a lesser extent in other tissues of the mouse and rat) by mechanisms not dependent upon direct interaction of the test chem. with DNA. Detection of 103 of the 115 carcinogens could be achieved by use of only male rats and female mice. Eleven of the 12 carcinogens that would be missed using this binary carcinogenicity bioassay protocol were carcinogenic in only a single tissue of a single sex of a single species, 4 being specific to the mouse liver. In contrast, use of only rats would fail to detect 34 mouse-specific carcinogens, 17 of which were active at sites other than

the liver, 7 at multiple sites. Thus screening chems. for genotoxicity using structural anal. and a min. no. of genotoxicity assays, and use of a reduced **cancer** bioassay protocol, would enable the detection of trans-species/multiple-site rodent carcinogens. The detection of tissue/sex/species-specific carcinogens can only be achieved by conducting life-time carcinogenicity bioassays according to the present NTP protocol. The transition over the past decade from selecting candidate chems. for bioassay based on consideration of chem. structure, to selection based on relative environmental importance, is sufficient to explain the apparent decreasing sensitivity of the Salmonella assay to rodent carcinogens.

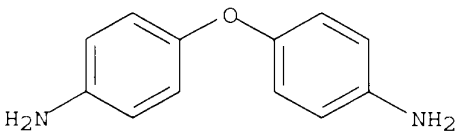
L8 ANSWER 68 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1987:641679 CAPLUS
DN 107:241679
TI 4,4'-Methylenebis(2-chloroaniline): an unregulated carcinogen
AU Ward, Elizabeth; Smith, Alexander Blair; Halperin, William
CS Div. Surveill, Hazard Eval. Field Stud., Natl. Inst. Occup. Saf. Health, Cincinnati, OH, 45226, USA
SO American Journal of Industrial Medicine (1987), 12(5), 537-49
CODEN: AJIMD8; ISSN: 0271-3586
DT Journal; General Review
LA English
IT **101-14-4**, MBOCA
RL: OCCU (Occurrence)
(carcinogenicity and legal status of)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



AB A review with many refs. on 4,4'-methylenebis(2-chloroaniline) (MBOCA), a confirmed animal carcinogen, which is used com. as a curing agent for polymers contg. isocyanate. There are no adequate studies documenting a carcinogenic risk for MBOCA in humans; however, MBOCA is structurally similar to arom. amines, which cause bladder **cancer** in workers with occupational exposure. Manuf. of MBOCA in the US ceased in 1979. An estd. 1400-33,000 workers were potentially exposed in the manuf. of MBOCA-cured products. There are no federal regulations limiting occupational exposure to MBOCA. NIOSH recommended in 1978 that MBOCA be treated as a potential human carcinogen and that worker exposure be controlled so that it does not exceed 3 .mu.g/m3 of air detd. as a time-weighted av. concn. for up to a 10-h workshift.

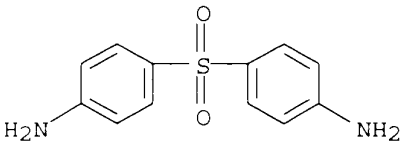
L8 ANSWER 69 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1987:570301 CAPLUS
DN 107:170301
TI Carcinogenic risk assessment: comparison of estimated safe doses for rats and mice
AU Chen, James J.; Gaylor, David W.
CS Natl. Cent. Toxicol. Res., Jefferson, AR, 72079, USA
SO Environmental Health Perspectives (1987), 72, 305-9

CODEN: EVHPAZ; ISSN: 0091-6765
DT Journal
LA English
IT **101-80-4**, 4,4'-Oxydianiline
RL: BIOL (Biological study)
(safe doses of, carcinogenicity and species in relation to)
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)

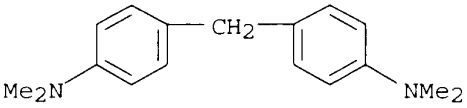


AB Data from the National **Cancer** Institute/National Toxicol. Program (NCI/NTP) carcinogenesis bioassays were examd. to compare **cancer** risks in rats and mice. Only those bioassays where chems. were administered orally were used. The ratios for rats-to-mice of the virtually safe dose (VSD) levels assocd. with a risk of 10-6 were compared. Comparisons of the ratios were made for those chems. that NCI/NTP detd. to be carcinogenic in .gtoreq.1 species and that showed a dose-response trend in the same sex at the same tissue/organ site in the other species. In all, 69 comparisons from 38 carcinogens were performed. The overall geometric mean of the VSD ratios is 1.27 in terms of concn. (ppm). The VSD ratios vary from 1:51 to 49:1. Without the restriction of the same sex and site, the geometric mean of the min. VSDs is 1.38. By directly comparing the VSDs for rats and mice (as they are performed for risk assessment), this study showed a probability of 0.10 that the ratio of VSDs is >10; and the ratio is >20 with a probability of 0.05 when a chem. is carcinogenic in both species.

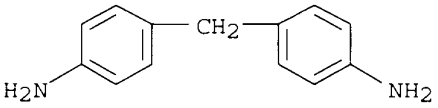
L8 ANSWER 70 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1987:491549 CAPLUS
DN 107:91549
TI Carcinogenicity of mutagens: predictive capability of the Salmonella mutagenesis assay for rodent carcinogenicity
AU Zeiger, Errol
CS Toxicol. Res. Test. Program, Natl. Inst. Environ. Health Sci., Research Triangle Park, NC, 27709, USA
SO Cancer Research (1987), 47(5), 1287-96
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
IT **80-08-0**, Dapsone **101-61-1**, 4,4'-Methylene-bis(N,N-dimethylaniline) **101-77-9**, 4,4'-Methylenedianiline **101-80-4**, 4,4'-Oxydianiline **139-65-1**, 4,4'-Thiodianiline
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(mutagenicity of, in Ames test, carcinogenicity predictability in relation to)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



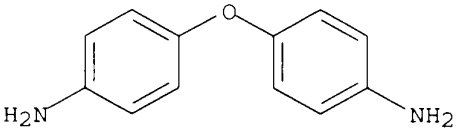
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



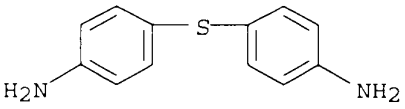
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



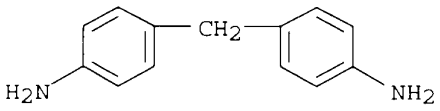
RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



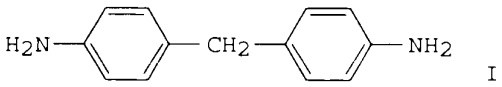
AB A total of 224 chem. that have been tested in long-term studies for carcinogenicity in rats and mice by the National **Cancer** Institute and the National Toxicol. Program were tested for mutagenicity in S. typhimurium. Correlations between mutagenicity and carcinogenicity were examd. The influences of chem. structure, rodent species, and organ responses, and bacterial strain responses on the carcinogenesis/mutagenesis correlations were also examd. Not all carcinogens induced tumors in both rats and mice. A clear mutagenic or equivocal mutagenic response in Salmonella was predictive for 77% of the

carcinogens or equivocal carcinogens, although only 54% of the 149 carcinogens or equivocal carcinogens were mutagens, and 58% of the nonmutagens were carcinogens or equivocal carcinogens. The proportion of mutagens and equivocal mutagens that were not carcinogenic or equivocal was 23%. There was no apparent way to distinguish the mutagenic carcinogens from the mutagenic noncarcinogens by the responses of the specific Salmonella strains. The proportions of different chem. classes in the data base strongly affected the correlations; 40% of the chlorinated carcinogens were mutagens. Because 29% of the chem. (30% of the carcinogens) were chlorinated, the poor correlation of this class was reflected in the overall correlation. The use of the Salmonella mutagenicity assay is warranted for the identification of carcinogens, but not for noncarcinogens. The proportion of carcinogens detected as mutagens is dependent on the specific classes of chem. tested and on the rodent species used to define the carcinogens.

L8 ANSWER 71 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1987:170802 CAPLUS
DN 106:170802
TI Current intelligence bulletin 47, 4,4'-methylenedianiline (MDA)
CS National Institute for Occupational Safety and Health, Cincinnati, OH, USA
SO Report (1986), DHHS/PUB/NIOSH-86-115; Order No. PB87-104527/GAR, 26 pp.
Avail.: NTIS
From: Gov. Rep. Announce. Index (U. S.) 1987, 87(2), Abstr. No. 703,004
DT Report
LA English
IT **101-77-9**, 4,4'-Methylenedianiline
RL: BIOL (Biological study)
(neoplasm from, of organ)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



GI

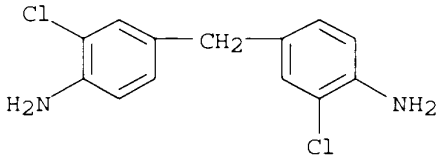


I

AB Wistar rats receiving a single injection of a tumor initiator 2,2'-dihydroxy-N-nitrosodipropylamine [53609-64-6] followed by MDA (I) [**101-77-9**] in the diet for 19 wk, developed thyroid follicular cell carcinomas and follicular cell and papillary adenomas. Fischer 344/N rats and B6C3F1 mice receiving MDA as the dihydrochloride ad libitum in drinking water for 2 yr developed thyroid follicular cell carcinomas and adenomas, C-cell adenomas of the thyroid, hepatocellular carcinomas and adenomas, alveolar bronchiolar adenomas, malignant lymphomas, and benign tumors of the adrenal gland. Workers with airborne and dermal exposure to powd. MDA developed toxic hepatitis. In addn., increased incidences of

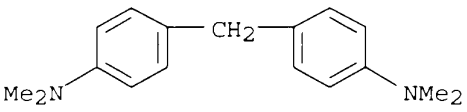
cancers of the bladder and large intestine and of lymphosarcoma and reticulosarcoma have been reported in workers with potential exposure to MDA.

L8 ANSWER 72 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1986:577747 CAPLUS
DN 105:177747
TI Prevention of occupation-related **cancers**
AU Anon.
CS Fr.
SO Cahiers de Notes Documentaires (1986), 124, 397
CODEN: CNDIBJ; ISSN: 0007-9952
DT Journal
LA French
IT **101-14-4**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(occupational exposure to, limit values for, in France)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)

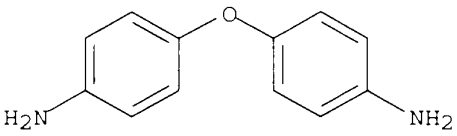


AB Mean exposure limit values for occupational exposure to chems. in France are presented for coal tar vapors, acrylonitrile [107-13-1], Be, N2H4, 4,4'-methylene-bis(2-chloroaniline) [**101-14-4**], Me2SO4 [77-78-1], and o-toluidine [95-53-4].

L8 ANSWER 73 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1986:455772 CAPLUS
DN 105:55772
TI Strain A mouse pulmonary tumor test results for chemicals previously tested in the National **Cancer** Institute carcinogenicity tests
AU Maronpot, R. R.; Shimkin, M. B.; Witschi, H. P.; Smith, L. H.; Cline, J. M.
CS Natl. Toxicol. Program, Natl. Inst. Environ. Health Sci., Research Triangle Park, NC, 27709, USA
SO JNCI, Journal of the National Cancer Institute (1986), 76(6), 1101-12
CODEN: JJIND8; ISSN: 0198-0157
DT Journal
LA English
IT **101-61-1 101-80-4**
RL: BIOL (Biological study)
(carcinogenicity and genotoxicity of, strain A mouse pulmonary tumor bioassay as screening test in relation to)
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)

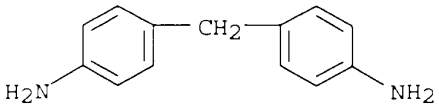


RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



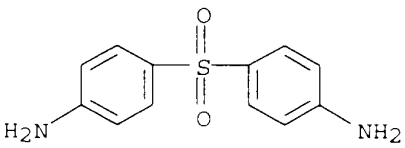
AB Sixty-five chems. were coded and examd. for their ability to induce lung tumors in strain A/St (lab. A) or strain A/J (lab. B) mice. Thirty-five chems. were tested in lab. A only, 6 in lab. B only, and 24 in both labs. Two-year carcinogenicity test results as well as genotoxicity test data are available for most of these chems. There was poor interlab. agreement in strain A test results for the 24 chems. tested in both labs. In addn., there was poor agreement between strain A test results from either lab. and 2-yr carcinogenicity test results or genotoxicity results. Possible explanations for these findings include selection of a large no. of arom. amines in the group of chems. submitted for strain A testing, differences in strain A testing protocols and in statistical anal. of results from the 2 labs., low sensitivity of the strain A/St mice used in this particular study, and general problems inherent in comparing any relatively short-term animal tumor model with 2-yr carcinogenicity tests. Since there is no abs. ref. for carcinogenicity, no one test system is better than another. Carcinogenicity test data are relevant only to the test model employed.

L8 ANSWER 74 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1986:179863 CAPLUS
DN 104:179863
TI Inhibitory effects of ethoxyquin, 4,4'-diaminodiphenylmethane and acetaminophen on rat hepatocarcinogenesis
AU Masui, Tsuneo; Tsuda, Hiroyuki; Inoue, Kazuhiko; Ogiso, Tadashi; Ito, Nobuyuki
CS Med. Sch., Nagoya City Univ., Nagoya, 467, Japan
SO Japanese Journal of Cancer Research (1986), 77(3), 231-7
CODEN: JJCREP; ISSN: 0910-5050
DT Journal
LA English
IT **101-77-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(neoplasm inhibitory activity of, in liver carcinogenesis)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)

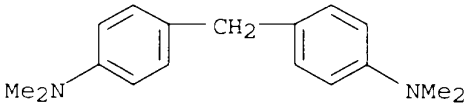


AB Four antioxidants, butylated hydroxyanisole (BHA) [25013-16-5], butylated hydroxytoluene (BHT) [128-37-0], ethoxyquin [91-53-2] and .alpha.-tocopherol [59-02-9], and 3 other compds., 4,4'-diaminodiphenylmethane (DDPM) [**101-77-9**], acetaminophen [103-90-2], and glutathione [70-18-8], were tested for inhibitory effect on hepatocarcinogenesis in male F344 rats. Rats were initially given a single i.p. injection of diethylnitrosamine (200 mg/kg body wt.) and fed a basal diet contg. 0.02% 2-acetylaminofluorene from week 2 to week 8. Animals were subjected to partial hepatectomy at the end of week 3. From week 12 to week 36, they were given basal diet contg. 2% BHA, 1% BHT, 0.8% ethoxyquin, 1% .alpha.-tocopherol, 0.1% DDPM, 1% acetaminophen, or 1% glutathione, then killed at week 40, 4 wk after cessation of treatment with the test chems. The incidence of hepatocellular carcinoma (HCC) was decreased in the groups given ethoxyquin or DDPM. Quant. anal. of the no. and area of HCC per unit liver area revealed a decrease in HCC in the groups given ethoxyquin, DDPM, or acetaminophen. Thus, ethoxyquin, DDPM and acetaminophen exerted an inhibitory effect on the development of HCC, while BHA, BHT, .alpha.-tocopherol, and glutathione had no effect.

L8 ANSWER 75 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1986:143623 CAPLUS
DN 104:143623
TI Reproducibility of microbial mutagenicity assays: II. Testing of carcinogens and noncarcinogens in Salmonella typhimurium and Escherichia coli
AU Dunkel, Virginia C.; Zeiger, Errol; Brusick, David; McCoy, Elena; McGregor, Douglas; Mortelmans, Kristien; Rosenkranz, Herbert S.; Simmon, Vincent F.
CS Natl. Cancer Inst., Natl. Inst. Health, Bethesda, MD, USA
SO Environmental Mutagenesis (1985), 7(Suppl. 5), 1-248
CODEN: ENMUDM; ISSN: 0192-2521
DT Journal
LA English
IT **80-08-0 101-61-1**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(mutagenicity of, in bacteria, assays for)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)

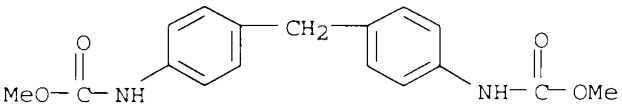


RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



AB A total of 63 chems were tested for mutagenicity in S. typhimurium strains TA 98, 100, 1535, 1537, and 1538, and E. coli WP2 uvrA in a 4-lab. study. Sixty of the chems. were tested for carcinogenicity by the National **Cancer** Institute or the National Toxicol. Program. All chems. were tested for mutagenicity without metabolic activation and with liver S-9 prepns. from uninduced and Aroclor 1254-induced F344 rats, B6C3F1 mice, and Syrian hamsters. The intra- and interlab. reproducibility of the Salmonella assay with regard to the overall judgment of mutagenic or nonmutagenic was good. The results in the E. coli strain, however, exhibited a high degree of variability between labs. With 1 or 2 exceptions, the mutagens were detected with S-9 prepns. from all 3 species. The uninduced liver S-9 prepns. did not activate any chems. to mutagens that were not also activated by induced S-9, but some chems. were detected as mutagens only when induced S-9 was used. A pos. mutagenic response in Salmonella was predictive of carcinogenicity 69% of the time; when equivocal carcinogens and borderline mutagens were included, the predictivity increased to 83%. Conversely, 76% of the carcinogens were mutagens. Relatively few chems. (18%) were mutagenic in E. Coli. Not all the carcinogens induced tumors in both rats and mice and the species specific carcinogenicity could not be predicted from the S-9 mutagenicity.

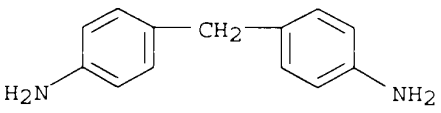
L8 ANSWER 76 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1985:571465 CAPLUS
DN 103:171465
TI Computer-assisted structure-anticancer activity correlations of carbamates and thiocarbamates
AU Nasr, Mohamed; Paull, Kenneth D.; Narayanan, V. L.
CS Starks C. P., Rockville, MD, 20852, USA
SO Journal of Pharmaceutical Sciences (1985), 74(8), 831-6
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
IT **7450-63-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm-inhibiting activity of, structure in relation to)
RN 7450-63-7 CAPLUS
CN Carbamic acid, (methylenedi-4,1-phenylene)bis-, dimethyl ester (9CI) (CA INDEX NAME)



AB With the aid of the computer, .apprx.8000 compds. that incorporate a carbamate or thiocarbamate moiety, which have been tested as potential anticancer agents at the National **Cancer** Institute (NCI), were classified and their structure-activity correlations against the in vivo

P-388 and L-1210 leukemias were evaluated. Arom. carbamates and thiocarbamates had good activity against P-388 and poor activity against L-1210. The majority of active compds. in this series of arom. carbamates possessed a 2- or 4-heteroatom-substituted Ph attached to the carbamate O atom or the thiocarbamate S atom with the carbamate N atom as NHMe. The N-Ph carbamates were much less active against P-388 than the Ph carbamates; only bis-N-Ph carbamates with a methylene bridge between the 2 Ph groups showed good activity against both P-388 and L-1210 leukemias. Except for the mycophenolic acid carbamates, the fused Ph carbamates showed poor activity against both P-388 and L-1210 leukemias. Certain N-heterocyclic carbamates and carbamates with heteroatom substituents were selected by the NCI for development toward clin. trials. The nature of the heterocyclic carrier and the position of attachment to the carbamate moiety have a major role on the mode of action of the antitumor activity of these compds.

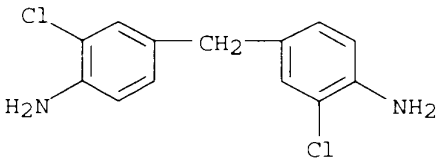
L8 ANSWER 77 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1985:565394 CAPLUS
DN 103:165394
TI The air toxics problem in the United States: an analysis of **cancer** risks for selected pollutants
AU Haemisegger, Elaine; Jones, Alan; Steigerwald, Bern; Thomson, Vivian
CS Off. Air Radiat., U. S. Environ. Prot. Agency, USA
SO U. S. Environ. Prot. Agency, Off. Air Qual. Plann. Stand., [Tech. Rep.] EPA (1985), EPA-450/1-85-001, 123 pp.
CODEN: UEPEDY
DT Report
LA English
IT **101-77-9**
RL: POL (Pollutant); OCCU (Occurrence)
(air pollution by, **cancer** risks in relation to exposure to, in US)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



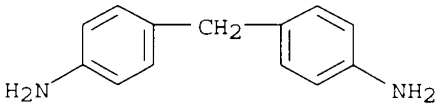
AB Both point sources and area sources contribute significantly to the air pollution problem in US. The important contributors to aggregate **cancer** incidence from toxic air pollutants include metals, asbestos, incomplete combustion products, gasoline vapors, and chlorinated org. compds. Max. lifetime individual risks of 10-4 (1 in 10,000) or greater in the vicinity of major points sources were estd. for 21 pollutants; of 10-3 (1 in 1000) or greater, for 13 pollutants.

L8 ANSWER 78 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1985:180526 CAPLUS
DN 102:180526
TI A quantum mechanical approach to the theory of **cancer** from polynuclear compounds. Metabolic activation and carcinogenicity of extended anilines and aminoazo compounds
AU Mohammad, S. Noor
CS Dep. Phys. Meteorol., Indian Inst. Technol., Kharagpur, 721302, India

SO Molecular Pharmacology (1985), 27(1), 148-55
CODEN: MOPMA3; ISSN: 0026-895X
DT Journal
LA English
IT **101-14-4 101-77-9**
RL: PROC (Process)
(carcinogenicity and metabolic activation of)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



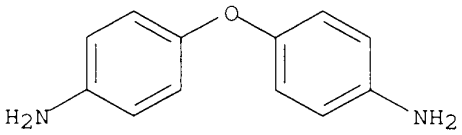
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



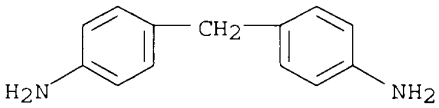
AB Calcns. were carried out of the electronic structure and mol. properties in relation to metabolic activation and carcinogenic activities of polycyclic arom. amines (PAAs). The quantum mech. MO method MINDO/3 is employed in the calcns. mainly on anilines, extended anilines, and aminoazo and other azo compds. The calcns., in agreement with findings of A. C. Arcos and M. F. Argus (1974), indicate that for the highest level of carcinogenic activity obtainable with the dicyclic arom. amines, the amino substituent must be introduced at the terminal C atom of the longest conjugate chain. In the case of monocyclic compds., in particular, charge distribution of the amino substitution aids in identifying the carcinogenic character of the PAAs. Thus, ring hydroxylation leads to detoxification of the compds. However, the major pathway leading to carcinogenic activity involves transformation to hydroxylamines and subsequently to electrophilic arylnitrenium ions (ANIs). These are in line with findings from expts. Calcns. of certain electronic parameters give expected relative carcinogenic potencies. In all cases the ANIs function as ambient electrophiles which can undergo both electrostatic and covalent binding with nucleophilic centers of proteins and DNA bases.

L8 ANSWER 79 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1985:144545 CAPLUS
DN 102:144545
TI Results from 86 two-year carcinogenicity studies conducted by the National Toxicology Program
AU Haseman, J. K.; Crawford, D. D.; Huff, J. E.; Boorman, G. A.; McConnell, E. E.
CS Natl. Inst. Environ. Health Sci., Research Triangle Park, NC, 27709, USA
SO Journal of Toxicology and Environmental Health (1984), 14(5-6), 621-39
CODEN: JTEHD6; ISSN: 0098-4108

DT Journal
LA English
IT **101-80-4 13552-44-8**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenicity of, assays for, administration route and sex and strain in relation to)
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



RN 13552-44-8 CAPLUS
CN Benzenamine, 4,4'-methylenebis-, dihydrochloride (9CI) (CA INDEX NAME)

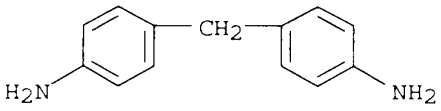


●2 HCl

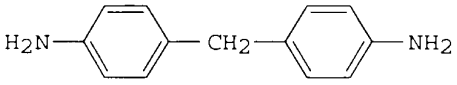
AB Five categories of evidence of carcinogenicity in rats and mice were used to group interpretative results on 86 chem. studied in carcinogenic tests carried out by the National Toxicol. Program. Of these studies, 50% were regarded as showing carcinogenic effects, 42% gave no evidence of carcinogenicity, 6% showed equivocal evidence of carcinogenicity, and 2% were regarded as inadequate expts. The liver was the most frequent site of **cancer** in rats and mice. Male rats appeared more sensitive than female rats to the induction of neoplasia; while for mice, the females seemed more responsive. The routes of administration yielding the highest percentage (80-83%) of pos. studies were gavage and inhalation; .apprx.1/3 of the feed, drinking water, and dermal studies showed carcinogenic effects. In feeding studies, overall survival in dosed and control groups were similar, while the majority of gavage studies showed significantly reduced survival in .gtoreq.1 dosed groups relative to the corresponding controls. The overall percentage of studies showing carcinogenic effects (50%) agrees closely with the rate reported by other investigators for nearly 200 earlier carcinogenicity expts. conducted by the National **Cancer** Institute.

L8 ANSWER 80 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1984:505513 CAPLUS
DN 101:105513
TI 4,4'-Diaminodiphenylmethane: promoting effect on the development of thyroid tumors in rats treated with N-bis(2-hydroxypropyl)nitrosamine
AU Hiasa, Yoshio; Kitahori, Yoshiteru; Enoki, Noboru; Konishi, Noboru; Shimoyama, Taketo
CS 1st. Dep. Pathol., Nara Med. Univ., Nara, 634, Japan

SO JNCI, Journal of the National Cancer Institute (1984), 72(2), 471-6
CODEN: JJIND8; ISSN: 0198-0157
DT Journal
LA English
IT **101-77-9**
RL: BIOL (Biological study)
(neoplasm promotion by, of kidney and thyroid gland, hydroxypropylnitrosamine in relation to)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



GI



I

AB 4,4'-Diaminodiphenylmethane (DDPM)(I) [**101-77-9**] promoted the development of thyroid tumors in rats treated with a subeffective dose of N-bis(2-hydroxypropyl)nitrosamine (DHPN) [53609-64-6] for thyroid tumorigenesis. Male inbred W rats were given a single i.p. injection of 280 mg DHPN/100 g and fed diets with or without 1000 ppm DDPM. Thyroid tumor incidences at the end of week 20 of the expt. were 90% (19/21) in rats given DHPN and then DDPM and 28% (6/21) in rats given DHPN alone. The incidence of thyroid **cancers** was 9.5% (2/21) in rats 1st given DHPN and then DDPM. Untreated rats and rats given DDPM alone had no thyroid tumors after 20 wk. Incidences of kidney tumors were 38% (8/21) in rats given DHPN and then DDPM and 28% (6/21) in rats given DHPN alone. No tumors were found in the kidneys and lungs of rats given DDPM alone and in those of control rats.

L8 ANSWER 81 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1984:466008 CAPLUS
DN 101:66008
TI Modulating the immune response system in mammals
IN Lang, Stanley Albert, Jr.; Fields, Thomas Lynn; Wilkinson, Raymond George; Kang, Soon Mok; Lin, Yank I.
PA American Cyanamid Co. , USA
SO Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 102476	A1	19840314	EP 1983-106543	19830705
	EP 102476	B1	19861105		

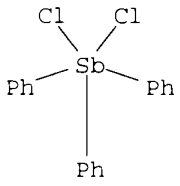
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE

and phenylsulfanylanilines I (R1 = H, Cl, or NO2; R2 = H or Cl; R3 = H, Br, Cl,Fl, NO2, C1-3 alkoxy, etc.; R4 and R5 = H or Cl; R6 = H or C1-3 alkyl; R7 = H, C1-3 alkyl, etc.; Z = S, SO, or SO2) is described for use as immune adjuvants. Some of the compds. were active in restoring antibody formation in mice with Rauscher virus-induced leukemia. The compds. may be useful for restoring immune function in **cancer**.

L8 ANSWER 82 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1983:438879 CAPLUS
DN 99:38879
TI Structural and biological characterization of antimony(V) polyamines
AU Carraher, Charles E., Jr.; Naas, Melissa D.; Giron, David J.; Cerutis, Delie Roselyn
CS Dep. Chem., Wright State Univ., Dayton, OH, 45435, USA
SO Journal of Macromolecular Science, Chemistry (1983), A19(8), 1101-20
CODEN: JMCHBD; ISSN: 0022-233X
DT Journal
LA English
IT **86368-93-6P 86368-94-7P 86369-02-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and structure and biol. characterization of)
RN 86368-93-6 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis-, polymer with dichlorotriphenylantimony (9CI) (CA INDEX NAME)

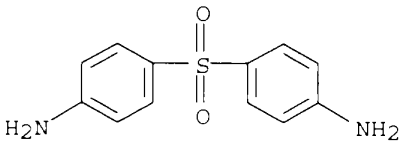
CM 1

CRN 594-31-0
CMF C18 H15 Cl2 Sb



CM 2

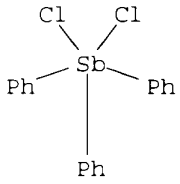
CRN 80-08-0
CMF C12 H12 N2 O2 S



RN 86368-94-7 CAPLUS
CN Benzenamine, 4,4'-methylenebis-, polymer with dichlorotriphenylantimony (9CI) (CA INDEX NAME)

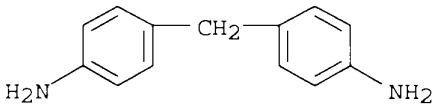
CM 1

CRN 594-31-0
CMF C18 H15 Cl2 Sb



CM 2

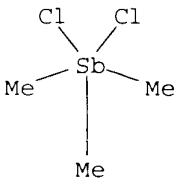
CRN 101-77-9
CMF C13 H14 N2



RN 86369-02-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis-, polymer with dichlorotrimethylantimony (9CI) (CA INDEX NAME)

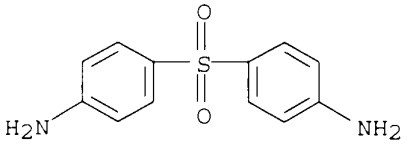
CM 1

CRN 13059-67-1
CMF C3 H9 Cl2 Sb



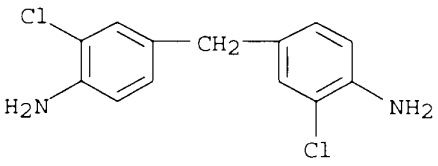
CM 2

CRN 80-08-0
CMF C12 H12 N2 O2 S

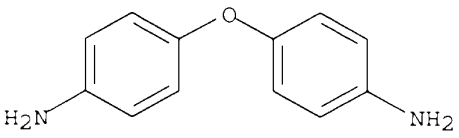


AB The condensation of organoantimony (V) dihalides with diamines forming Sb (V) polyamines employing the interfacial technique is described. Structural characterization of accomplished by elemental anal., light-scattering photometry, IR spectroscopy, control reactions, and mass spectroscopy. The products exhibited mild inhibition to a wide range of bacteria and to HeLa, BHK-21, and L929 **cancer**-related cell lines.

L8 ANSWER 83 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1983:1469 CAPLUS
DN 98:1469
TI Availability of epidemiologic data on humans exposed to animal carcinogens. II. Chemical uses and production volume
AU Karstadt, Myra; Bobal, Renee
CS Mt. Sinai Sch. Med., City Univ. New York, New York, NY, USA
SO Teratogenesis, Carcinogenesis, and Mutagenesis (1982), 2(2), 151-67
CODEN: TCMUD8; ISSN: 0270-3211
DT Journal
LA English
IT **101-14-4 101-80-4**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenicity of, human epidemiol. of, prodn. vol. and usage in relation to)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



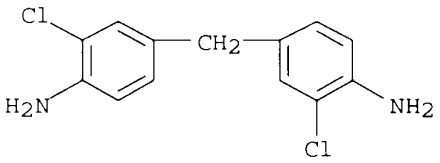
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



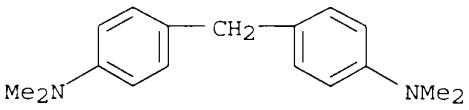
AB Data on the prodn. and marketing vols. of 75 substances classified as carcinogens by the International Agency for Research on **Cancer** (IARC) is presented. A few epidemiol. studies from the companies marketing or using any of the 75 IARC carcinogens are presented and

discussed; most companies, however, did not conduct such studies due to small work forces, difficulty in tracing workers, and reduced usage and(or) prodn. among other reasons. It is suggested that epidemiol. studies involving users of IARC carcinogens rather than producers be conducted.

L8 ANSWER 84 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1982:576686 CAPLUS
DN 97:176686
TI Reliability of the hepatocyte primary culture/DNA repair test in testing of coded carcinogens and noncarcinogens
AU Williams, G. M.; Laspia, M. F.; Dunkel, V. C.
CS Naylor Dana Inst. Dis. Prevent., Am. Health Found., Valhalla, NY, 10595, USA
SO Mutation Research (1982), 97(5), 359-70
CODEN: MUREAV; ISSN: 0027-5107
DT Journal
LA English
IT **101-14-4 101-61-1**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenicity of, by hepatocyte/DNA repair test)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



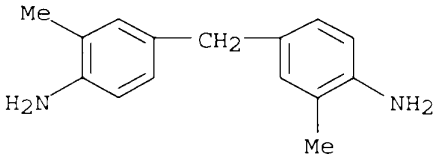
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



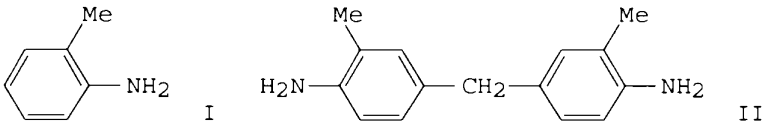
AB The hepatocyte primary culture/DNA repair test was evaluated for its reliability using a series of coded samples. Among the 30 chems. tested, 15 were general ref. compds. and 15 were chems. that were tested for carcinogenicity in the U.S. National **Cancer** Institute (NCI) Bioassay Program. The latter group were from the same lot that had been used for the in vivo testing and mutagenicity in the Ames test. From the group of 15 ref. compds., 5 were pos. for DNA repair and carcinogens. Of the 10 samples scored as neg., 4 were noncarcinogens and 6 carcinogens. Among the 6 carcinogens were 3 compds. whose carcinogenicity probably does not involve the prodn. of DNA damage. From the 15 coded chems. that were tested for carcinogenicity by the NCI in long-term animal studies, 7 were scored as pos. 5 Of these were judged carcinogenic in the in vivo bioassays and the other 2, which were also mutagenic in Salmonella, showed some indication of carcinogenicity. Of the 8 compds. that were scored as neg., 5 were noncarcinogenic. Among the 3 carcinogens that were not

detected, there was at least 1 whose carcinogenicity probably does not involve DNA damage. Thus, pos. results in the hepatocyte primary culture/DNA repair test are highly specific for carcinogens and the test is also highly sensitive in the detection of DNA-damaging genotoxic carcinogens.

L8 ANSWER 85 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1982:194902 CAPLUS
DN 96:194902
TI The carcinogenic effect of aromatic amines: an epidemiological study on the role of o-toluidine and 4,4'-methylenebis[2-methylaniline] in inducing bladder **cancer** in man
AU Rubino, Giovanni F.; Scansetti, Giovanni; Piolatto, Giorgio; Pira, Enrico
CS Inst. Occup. Health, Turin Univ., Turin, 29-10126, Italy
SO Environmental Research (1982), 27(2), 241-54
CODEN: ENVRAL; ISSN: 0013-9351
DT Journal
LA English
IT **838-88-0**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenicity of, to human bladder, dyestuff manufg. in relation to)
RN 838-88-0 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-methyl- (9CI) (CA INDEX NAME)



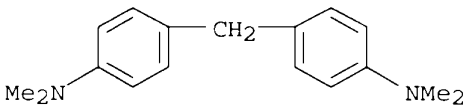
GI



AB Cause-specific mortality of 906 workers 1st employed 1922-1970 in a dyestuff factory in Northern Italy was compared to national figures; where a marked excess of bladder **cancer** was obsd. (36 obsd. vs. 1.23 expected deaths). The mean latent period was 25 yr. The excess was higher among those with longer duration of exposure. Some excess of mortality from lung **cancer**, laryngeal **cancer**, and esophageal **cancer** was also found, but a clear explanation could not be provided regarding the causal role of arom. amines. Mortality from bladder **cancer** was very much higher among those exposed in benzidine and naphthylamines manuf. as compared to those only exposed in use or intermittent contact. Excess bladder **cancer** was also very high among workers in fuchsin manuf. There is evidence that o-toluidine (I) [95-53-4] and 4,4'-methylenebis[2-methylaniline] (II) [**838-88-0**] should be implicated in such excess mortality. Caution

in handling these compds. is therefore suggested and the need for further studies to confirm such findings is stressed.

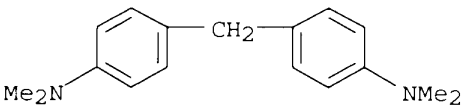
L8 ANSWER 86 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1980:598975 CAPLUS
DN 93:198975
TI Mutagenic activity of chemicals previously tested for carcinogenicity in the National **Cancer** Institute bioassay program
AU Dunkel, V. C.; Simmon, V. F.
CS Natl. Cancer Inst., Bethesda, MD, USA
SO IARC Scientific Publications (1980), 27(Mol. Cell. Aspects Carcinog. Screening Tests), 283-302
CODEN: IARCCD; ISSN: 0300-5038
DT Journal
LA English
IT **101-61-1**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (mutagenicity of, carcinogenicity in relation to)
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



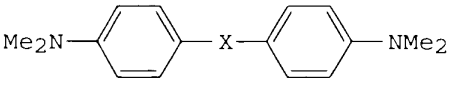
AB The Salmonella/microsome plate assay was used for screening 26 different chems. for their mutagenicity. 3-Nitropropionic acid [504-88-1], 4-nitro-o-phenylenediamine [99-56-9], and p-phenylenediamine [106-50-3] were not carcinogenic, but were pos. in the mutagenicity assay. Of the 13 chem. tested in long-term animal bioassays as carcinogenic, 6 were mutagenically-active without metabolic activation (4-amino-2-nitrophenol [119-34-6], 2-nitro-p-phenylenediamine [5307-14-2], 2-amino-5-nitrothiazole [121-66-4], 3-chloromethyl pyridine-HCl [6959-48-4], 1,5-naphthalenediamine [2243-62-1], and ethylene dibromide [106-93-4]). 4,4'-Bis(dimethylamino)benzophenone [90-94-8], 4,4'-methylenebis(N,N-dimethylaniline) [**101-61-1**], tris(2,3-dibromopropyl) phosphate [126-72-7], and o-anisidine-HCl [134-29-2] induced varying mutagenic response only with metabolic activation. Cinnamyl anthranilate [87-29-6], nitrilotriacetic acid tri-Na salt [5064-31-3], and reserpine [50-55-5] were carcinogenic in animals but not mutagenic in the bacterial assay. p-Chloroaniline [106-47-8], 1,2,3-benzotriazole [95-14-7], proflavine-HCl [7459-75-8], and styrene [100-42-5] were designated as suspect for carcinogenicity. With the exception of styrene, the other 3 compds. were mutagenic. Aspirin-phenacetin-caffeine mixt. (50:46:4) was not mutagenic.

L8 ANSWER 87 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1980:401979 CAPLUS
DN 93:1979
TI Binding of the dye intermediates Michler's ketone and methane base to rat liver nucleic acids and lack of mutagenicity in Salmonella typhimurium
AU Scribner, John D.; Koponen, Gertrud; Fisk, Sharon R.; Woodworth, Becky
CS Pac. Northwest Res. Found., Seattle, WA, 98104, USA
SO Cancer Letters (Shannon, Ireland) (1980), 9(2), 117-21
CODEN: CALEDQ; ISSN: 0304-3835

DT Journal
LA English
IT **101-61-1**
RL: BIOL (Biological study)
(DNA binding by, carcinogenicity indication in relation to)
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



GI

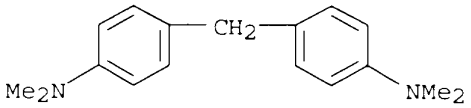


I, X=CO
II, X=CH_2

AB Tritiated Michler's ketone (I) [90-94-8] (a hepatocarcinogen) or methane base (II) [**101-61-1**] (nonhepatocarcinogen) were injected into male rats. The rats were killed and the liver nucleic acids were isolated. Initial binding of I (18 h) to DNA was .apprx.1/3 of 2-acetamidofluorene (AAF) [53-96-3], but was more persistent than AAF binding. Initial binding of II was .apprx.1/3 of I. Six weeks after injection of I, the amt. bound to DNA was the same as at 3 days, while the binding to RNA had dropped to an insignificant level. Both I and II were nonmutagenic on S. typhimurium with rat liver activating enzyme at 4-400 .mu.g/35-mm plate, while 4 .mu.g/plate of AAF produced more than 300 revertants in each of the tester strains. Thus, hepatocarcinogenicity of I, II, and AAF in male rats was correlated with chem. binding of metabolites to liver DNA and RNA, but I failed to produce mutations in S. typhimurium even in the presence of activating enzymes from the target tissue. I was inactivated in the Ames assay, but did attack nucleic acids in the livers of whole animals, to an extent correlated with the carcinogenic activity found in the National **Cancer** Institute bioassay. Thus, where feasible, in vivo binding expts. may be a more reliable indicator of potential carcinogenicity than bacterial mutagenicity assays.

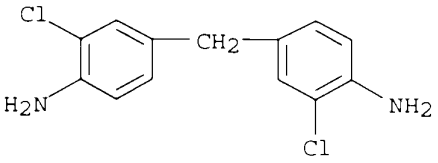
L8 ANSWER 88 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1979:414967 CAPLUS
DN 91:14967
TI Selection of carcinogens and related compounds tested for mutagenic activity
AU Poirier, Lionel A.; Weisburger, Elizabeth K.
CS Natl. Cancer Inst., NIH, Bethesda, MD, 20014, USA
SO Journal of the National Cancer Institute (1940-1978) (1979), 62(4), 833-40
CODEN: JNCIAM; ISSN: 0027-8874
DT Journal
LA English
IT **101-61-1**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(carcinogenicity of, mutagenicity in relation to)
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)



AB A list of 102 chems. was prepd. for subsequent mutagenesis assays in a National **Cancer** Institute program to det. the extent of correlation between carcinogenesis and mutagenesis in standardized assays. The chems. were divided into 5 major categories: 37 arom. amines, 11 polycyclic arom. hydrocarbons, 8 nitrosamines and nitrosamides, 16 alkylating agents, and a misc. category consisting of 11 heterocyclic compds., 7 amides, ureas and acylating agents, 5 antimetabolites, 4 inorg. chems., and 3 promoters. The chems. were further described as procarcinogens (requiring metabolic activation to exert their biologic activities), ultimate carcinogens (direct-acting chems. not requiring metabolic activation), and noncarcinogens (compds. shown to be inactive in one or more adequate carcinogenicity tests). An extensive bibliog. documents the selection and categorization of the compds.

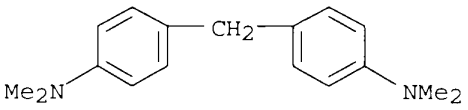
L8 ANSWER 89 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1978:585184 CAPLUS
DN 89:185184
TI Decontamination of aromatic amine **cancer**-suspect agents on concrete, metal, or painted surfaces
AU Weeks, R. W., Jr.; Dean, B. J.
CS Ind. Hyg. Group, Los Alamos Sci. Lab., Los Alamos, NM, USA
SO American Industrial Hygiene Association Journal (1958-1999) (1978), 39(9), 758-62
CODEN: AIHAAP; ISSN: 0002-8894
DT Journal
LA English
IT **101-14-4**
RL: OCCU (Occurrence)
(spills, on concrete and metal and painted surfaces, decontamination of)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



AB Phys. and chem. methods for removal of amines, e.g., Moca [**101-14-4**], benzidine [92-87-5], 3,3'-dichlorobenzidine [91-94-1], .alpha.-naphthylamine [134-32-7], .beta.-naphthylamine [91-59-8], and 4-aminobiphenyl [92-67-1], are described. Chem. removal includes transforming the amine to its MeOH-sol. Schiff base. It is

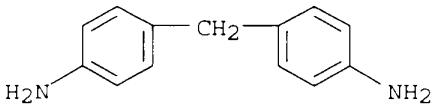
recommended that concrete and wood surfaces in chem. work areas be painted with a nonpermeable paint to minimize health hazards.

L8 ANSWER 90 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1978:34070 CAPLUS
DN 88:34070
TI Tetrabase, an alternative to benzidine and orthotolidine for detection of hemoglobin in urine
AU Lomholt, Bodil; Keiding, Niels
CS Inst. Med. Genet., Univ. Copenhagen, Copenhagen, Den.
SO Lancet (1977), 8011, 608-9
CODEN: LANCAO; ISSN: 0140-6736
DT Journal
LA English
IT **101-61-1**
RL: ANST (Analytical study)
(Hb detn. with, in urine)
RN 101-61-1 CAPLUS
CN Benzenamine, 4,4'-methylenebis[N,N-dimethyl- (9CI) (CA INDEX NAME)

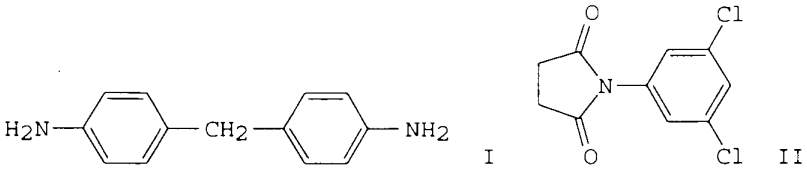


AB Hb was detected in urine samples by using a reagent contg. 20 g Tetrabase (N,N'-tetramethyldiaminodiphenylmethane), 400 mL HOAc, 1 mL 30% H2O2 dild. with 200 mL H2O, 27 mL 25% NH4OH dild. with 54 mL H2O, all dild. with 340 mL H2O. After reaction of the reagent with urine, the blue-green color was detd. at 605 nm. Hb was also detd. by the cyanomethemoglobin method. Intra-individual variation had a relative std. deviation of 1.3%; the Tetrabase method has a relative std. deviation of .apprx.10% which meets the requirements of routine work. Tetrabase has failed to produce **cancer** in mice and is suggested as a substitute for benzidine.

L8 ANSWER 91 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1977:497080 CAPLUS
DN 87:97080
TI Effect of hepatotoxic or nephrotoxic agents on the induction of colon **cancers** in rats by 1,2-dimethylhydrazine
AU Fukushima, Shoji; Hibino, Tsutomu; Shibata, Michiko; Murasaki, Geni; Ogiso, Tadashi; Ito, Nobuyuki
CS Sch. Med. Technol. Nursing, Nagoya Hoken-Eisei Univ., Aichi, Japan
SO Toxicology and Applied Pharmacology (1977), 40(3), 561-70
CODEN: TXAPA9; ISSN: 0041-008X
DT Journal
LA English
IT **101-77-9**
RL: BIOL (Biological study)
(liver injury from, colon **cancers** from dimethylhydrazine in relation to)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)

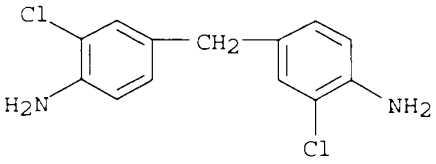


GI

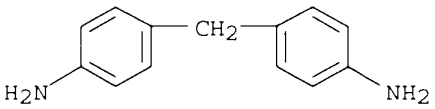


AB The effects of liver injury induced by p,p'-diaminodiphenylmethane (I) [**101-77-9**] and of kidney injury induced by N-(3,5-dichlorophenyl)succinimide (II) [24096-53-5] on 1,2-dimethylhydrazine (DMH) [540-73-8] colon carcinogenesis were examd. in rats. Prior administration of either I or II before DMH injection resulted in no significant differences in tumor incidences, but differences were noted in histol. pattern, tumor size, and extent of invasion.

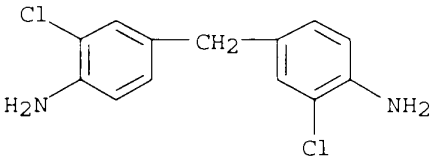
L8 ANSWER 92 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1977:50309 CAPLUS
DN 86:50309
TI Detection limits of chemical spot tests toward certain carcinogens on metal, painted, and concrete surfaces
AU Weeks, R. W., Jr.; Dean, B. J.; Yasuda, S. K.
CS Los Alamos Sci. Lab., Univ. California, Los Alamos, NM, USA
SO Analytical Chemistry (1976), 48(14), 2227-33
CODEN: ANCHAM; ISSN: 0003-2700
DT Journal
LA English
IT **101-14-4 101-77-9**
RL: ANT (Analyte); ANST (Analytical study)
(detection of, on concrete and metal and painted surfaces)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



IT **101-14-4**
RL: ANT (Analyte); ANST (Analytical study)
(detection of, on concrete and metal and painted surfaces, detection limits of spot tests for)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)

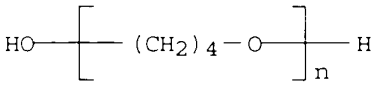


AB The formation of chromogenic and fluorogenic derivs. of certain arom. amines designated by The Occupational/Safety and Health Administration as **cancer**-suspect agents has allowed these compds. to be detected at very low levels through chem. spot tests. Well-defined painted, metal, and concrete surfaces were used as std. surfaces to evaluate the limit of detection values of these compds. as a function of both the visualization reagent and the method of detection. The chromogenic reagent of choice was Ehrlich's reagent and the fluorogenic reagents were either fluorescamine [38183-12-9] or o-phthalaldehyde [643-79-8]. The limit of detection values for these compds. in terms of grams of analyte/cm2 of surface being analyzed ranged from the low nanogram to 5-.mu.g level depending upon the compd., sampling technique, and surface involved. The combination of sampling technique and visualization reagent employed extend the limit of detection to levels considerably lower than previously reported.

L8 ANSWER 93 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1976:587521 CAPLUS
DN 85:187521
TI Carcinogenic activity of a chlorinated polyether polyurethan
AU Autian, J.; Singh, A. R.; Turner, J. E.; Hung, G. W. C.; Nunez, L. J.; Lawrence, W. H.
CS Cent. Health Sci., Univ. Tennessee, Memphis, TN, USA
SO Cancer Research (1976), 36(11, Pt. 1), 3973-7
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
IT **56641-03-3**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenicity of, after implantation)
RN 56641-03-3 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro-, polymer with 1,4-diisocyanato-2-methylbenzene and .alpha.-hydro-.omega.-hydroxypoly(oxy-1,4-butanediyl) (9CI) (CA INDEX NAME)

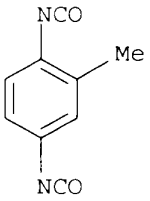
CM 1

CRN 25190-06-1
CMF (C4 H8 O)n H2 O
CCI PMS



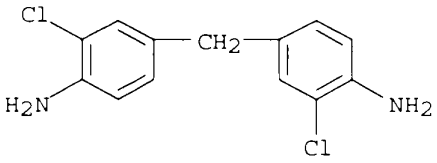
CM 2

CRN 614-90-4
CMF C9 H6 N2 O2



CM 3

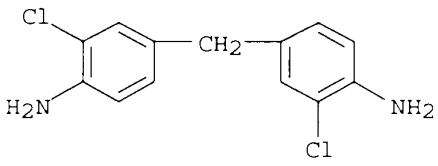
CRN 101-14-4
CMF C13 H12 Cl2 N2



AB On the basis of the results of an earlier study, a particular Y-238 (polyurethane) [**56641-03-3**] sample was selected for further evaluation of its carcinogenic potential. This sample was subjected to phys. and chem. tests for elucidation of its chem. structure, mol. wt., and mol. wt. distribution. Addnl. biol. tests were conducted on male NBR rats by implanting various quantities of the sample i.p., while others received an intrabronchus implant. Tumors, assessed histol. as milignant, were obsd. following both routes of implantation. The most common neoplasm of the pulmonary site was epidermoid carcinoma, whereas fibrosarcoma was the most common neoplasm in the peritoneal cavity. Data from the i.p. implantation suggested a dose-related incidence of **cancers**.

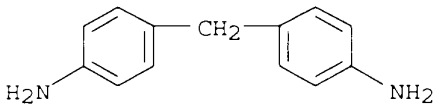
L8 ANSWER 94 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1972:424422 CAPLUS

DN 77:24422
TI 4,4'-Methylenebis(2-chloroaniline) (MOCA). Evaluation of hazards and exposure control
AU Linch, Adrian L.; O'Connor, George B.; Barnes, John R.; Killian, A. Stanley, Jr.; Neeld, W. E., Jr.
CS Chambers Works, E. I. du Pont de Nemours and Co., Inc., Deepwater, NJ, USA
SO American Industrial Hygiene Association Journal (1958-1999) (1971), 32(12), 802-19
CODEN: AIHAAP; ISSN: 0002-8894
DT Journal
LA English
IT **101-14-4**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (health hazards of)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



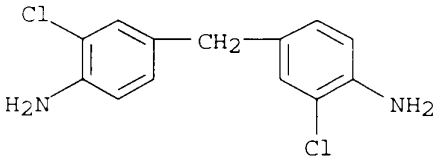
AB Procedures are outlined for a direct, accurate, and sp. gas chromatog. detn. of MOCA in urine and in air at concns. of 40 ppb and 10 .mu.g/m3, resp. During 16 years of exposure to MOCA (used as a curing agent for isocyanate-contg. polymers and epoxy systems) the operators and mechanics assigned to the manufg. area showed no symptoms derived from MOCA even through a high incidence in liver **cancer** is reported for rats fed MOCA in a protein-deficient diet. Dogs showed no malignancy during the 3rd year of a 6 year MOCA feeding study. Under industrial hygiene controls used in the production area, no cyanosis-anemia syndrome was obsd. Skin absorption from direct contact was a major source of MOCA absorption by workers.

L8 ANSWER 95 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1970:443172 CAPLUS
DN 73:43172
TI Carcinogenic activity of 4,4'-diaminodiphenylmethane and 2,4'-diaminodiphenylmethane
AU Steinhoff, Dieter; Grundmann, E.
CS Inst. Exptl. Pathol., Farbenfabriken Bayer A.-G., Wuppertal-Elberfeld, Fed. Rep. Ger.
SO Naturwissenschaften (1970), 57(5), 247-8
CODEN: NATWAY; ISSN: 0028-1042
DT Journal
LA German
IT **101-77-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (carcinogenic activity of)
RN 101-77-9 CAPLUS
CN Benzenamine, 4,4'-methylenebis- (9CI) (CA INDEX NAME)



AB 4,4'- (I) and 2,4'-Diaminodiphenylmethane (II) were applied s.c. to rats at 1.41 g/kg (LD50 200 mg/kg) and 7.3 g/kg (LD50 3300 mg/kg) doses, resp. I was slightly cancerogenic (50% of the rats died of **cancer** as compared with 26% of rats treated with physiol. saline). I also possessed hepatotropic activity. II had no cancerogenic activity in rats.

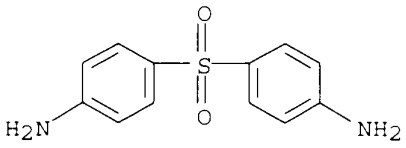
L8 ANSWER 96 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1970:65463 CAPLUS
DN 72:65463
TI Food additives. 4,4'-Methylenebis(2-chloroaniline)
AU Anon.
SO Federal Register (1969), 34(230), 19073-4, 2 Dec 1969
CODEN: FEREAC; ISSN: 0097-6326
DT Journal
LA English
IT **101-14-4**
RL: BIOL (Biological study)
(food additive, standards for)
RN 101-14-4 CAPLUS
CN Benzenamine, 4,4'-methylenebis[2-chloro- (9CI) (CA INDEX NAME)



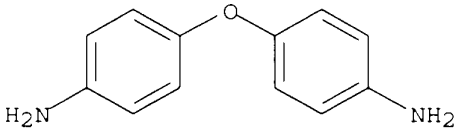
AB Since the title compd. induces **cancer** when ingested by test animals, the regulations under the U.S. Federal Food, Drug, and Cosmetic Act for food-contacting adhesives and polyurethane resins are amended to delete the use of this compd. as a component.

L8 ANSWER 97 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1968:409358 CAPLUS
DN 69:9358
TI the carcinogenicity of multIUCtion of brain tumors.ang. s.ang.
AU Griswold, Daniel P., Jr.; Casey, Albert E.; Weisburger, Elizabeth K.; Weisburger, J. H.
CS Southern Res. Inst., Birmingham, AL, USA
SO Cancer Research (1968), 28(5), 924-33
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
IT **80-08-0 101-80-4 139-65-1 4987-97-7 13552-44-8**
RL: PROC (Process)
(carcinogenic action of)
RN 80-08-0 CAPLUS

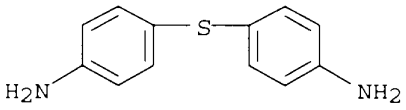
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)



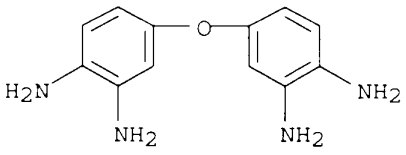
RN 101-80-4 CAPLUS
CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



RN 139-65-1 CAPLUS
CN Benzenamine, 4,4'-thiobis- (9CI) (CA INDEX NAME)



RN 4987-97-7 CAPLUS
CN 1,2-Benzenediamine, 4,4'-oxybis-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

RN 13552-44-8 CAPLUS
CN Benzenamine, 4,4'-methylenebis-, dihydrochloride (9CI) (CA INDEX NAME)

this is not only due to the described 'Pandora's box' situation. At least three other factors are described. Firstly, in the industrial world the medical treatment of **cancer** in patients occurs with high levels of extremely mutagenic agents. Actually, both in no. of persons and in exposure levels such medical treatment is the single largest exposure of humans to known carcinogens. Although such treatments are very effective in curing the tumor as present in the patient, the recurrence of **cancer** in those patients later in life is very high. In other words: "curing **cancer** is not the same as preventing **cancer** death in the human population". Secondly, the rate of **cancer** death in the human population is also detd. by the efficacy in which other major causes of death are prevented. For instance, cardiovascular diseases are the major cause of death in humans in the industrialized world. There is evidence that the treatment of cardiovascular diseases is more successful than that of **cancer**. On a population level this will result in increase of **cancer** being the ultimate death cause. Finally, the improvement of medical treatment of diseases together with an improved quality of life will lead to increase av. age of the population. Because the onset of most **cancer** is long after the exposure to carcinogens-in human often more than 30 yr-**cancer** is predominantly a disease of the old age. This means that if the av. age of human increases, there will be a selective preference of **cancer** becoming an even more important cause of death. This esp. will be pronounced in those countries were the age distribution in a population is abnormal.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1999:425745 CAPLUS
DN 131:87909
TI Inhibition of p38 kinase activity using substituted heterocyclic ureas
IN Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko
PA Bayer Corporation, USA
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9932111	A1	19990701	WO 1998-US26080	19981222
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	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
				US 1997-995750 A	19971222
	CA 2315720	AA	19990701	CA 1998-2315720	19981222
				US 1997-995750 A	19971222
				WO 1998-US26080W	19981222
	AU 9919971	A1	19990712	AU 1999-19971	19981222
	AU 739642	B2	20011018		

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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DE 2000-10038007A 20000804

DE 10038007	A1	20020214	DE 2000-10038007 20000804
AU 2001078502	A5	20020218	AU 2001-78502 20010723
			DE 2000-10038007A 20000804
			WO 2001-EP8477 W 20010723
US 2003027862	A1	20030206	US 2001-918741 20010731
			DE 2000-10038007A 20000804

OS MARPAT 136:183619

IT **398522-50-4P 398522-51-5P 398522-52-6P**
398522-53-7P 398522-54-8P 398522-55-9P
398522-56-0P 398522-57-1P 398522-58-2P
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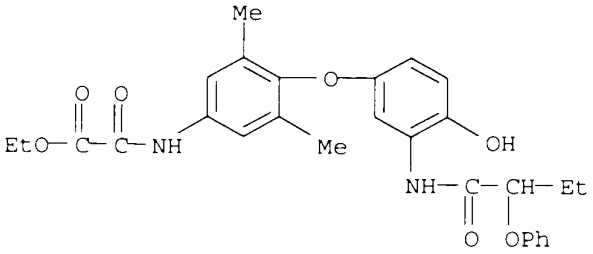
398524-04-4P 398524-05-5P 398524-06-6P
398524-09-9P 398524-11-3P 398524-12-4P
398524-13-5P 398524-15-7P 398524-17-9P
398524-18-0P 398524-19-1P 398524-20-4P
398524-21-5P 398524-22-6P 398524-24-8P
398524-26-0P 398524-28-2P 398524-29-3P
398524-30-6P 398524-35-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of di-Ph ether amides, oxamides, and ureas for treatment of arteriosclerosis and hypercholesterolemia)

RN 398522-50-4 CAPLUS

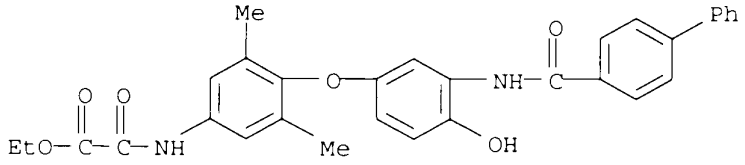
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxo-2-phenoxybutyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



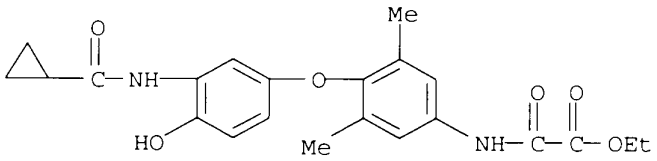
RN 398522-51-5 CAPLUS

CN Acetic acid, [[4-[3-[([1,1'-biphenyl]-4-ylcarbonyl)amino]-4-

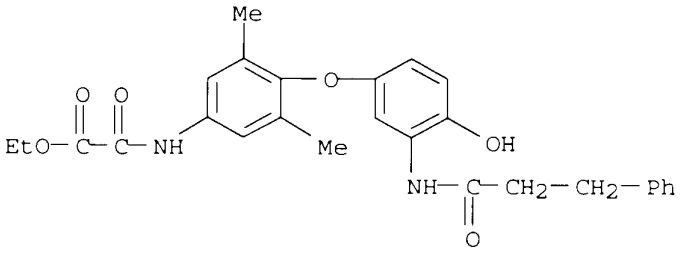
hydroxyphenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



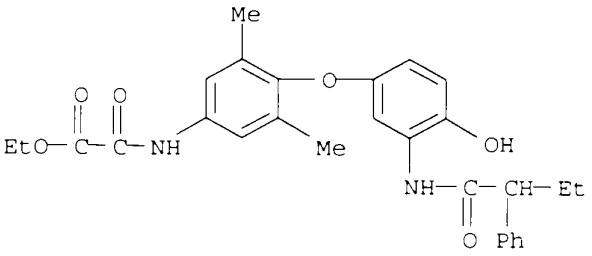
RN 398522-52-6 CAPLUS
CN Acetic acid, [[4-[3-[(cyclopropylcarbonyl)amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



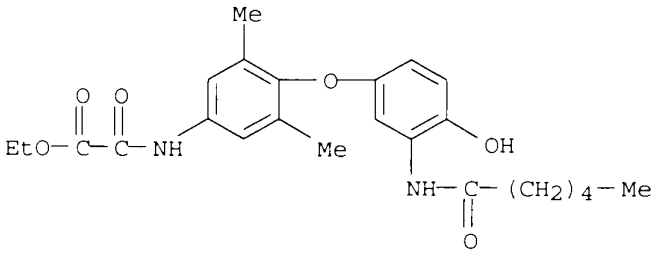
RN 398522-53-7 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxo-3-phenylpropyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



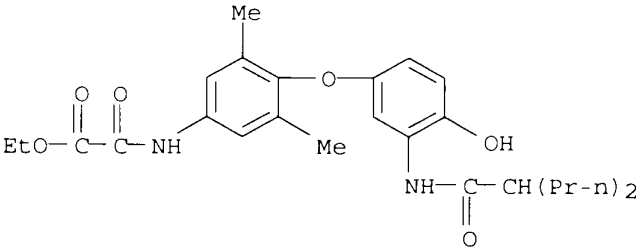
RN 398522-54-8 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxo-2-phenylbutyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



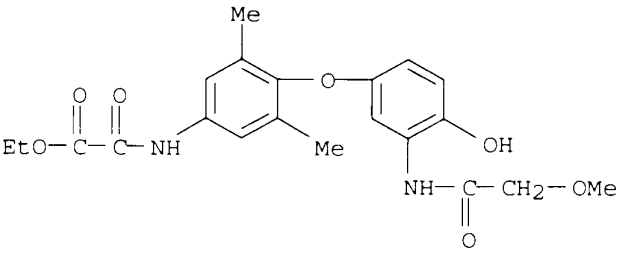
RN 398522-55-9 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxohexyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



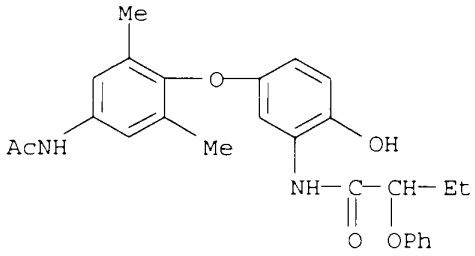
RN 398522-56-0 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxo-2-propylpentyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



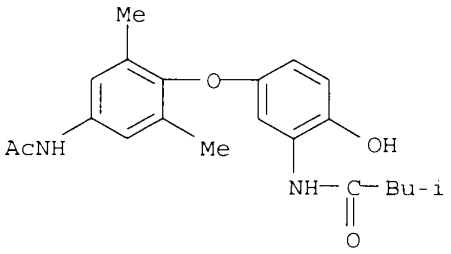
RN 398522-57-1 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(methoxyacetyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



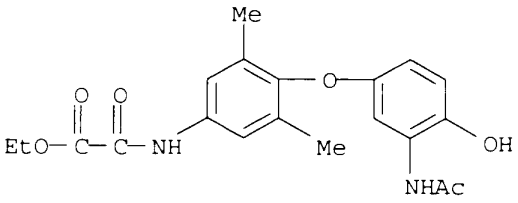
RN 398522-58-2 CAPLUS
CN Butanamide, N-[5-[4-(acetylamino)-2,6-dimethylphenoxy]-2-hydroxyphenyl]-2-phenoxy- (9CI) (CA INDEX NAME)



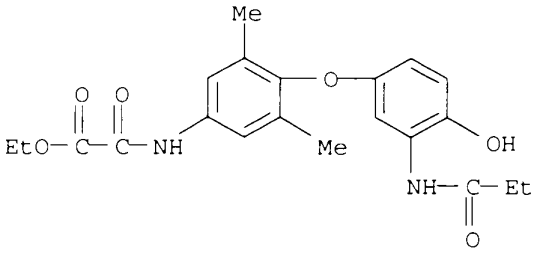
RN 398523-67-6 CAPLUS
CN Butanamide, N-[5-[4-(acetylamino)-2,6-dimethylphenoxy]-2-hydroxyphenyl]-3-methyl- (9CI) (CA INDEX NAME)



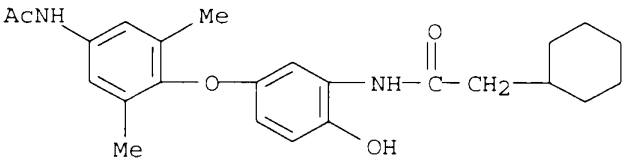
RN 398523-71-2 CAPLUS
CN Acetic acid, [[4-[3-(acetylamino)-4-hydroxyphenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



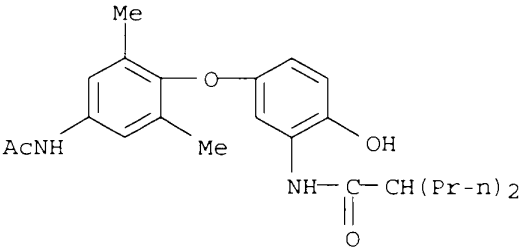
RN 398523-74-5 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxopropyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



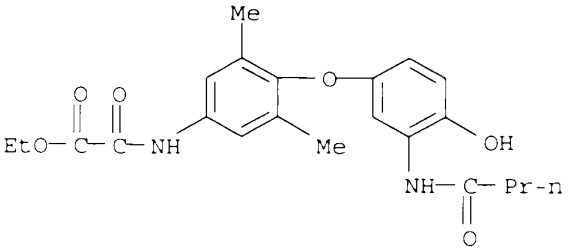
RN 398523-76-7 CAPLUS
CN Cyclohexaneacetamide, N-[5-[4-(acetylamino)-2,6-dimethylphenoxy]-2-hydroxyphenyl]- (9CI) (CA INDEX NAME)



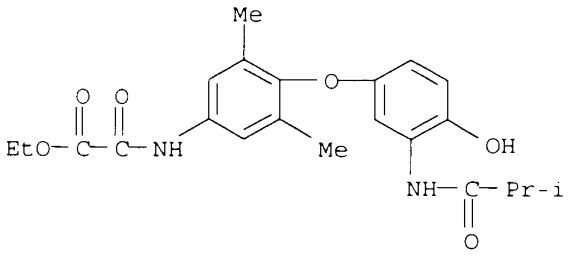
RN 398523-78-9 CAPLUS
CN Pentanamide, N-[5-[4-(acetylamino)-2,6-dimethylphenoxy]-2-hydroxyphenyl]-2-propyl- (9CI) (CA INDEX NAME)



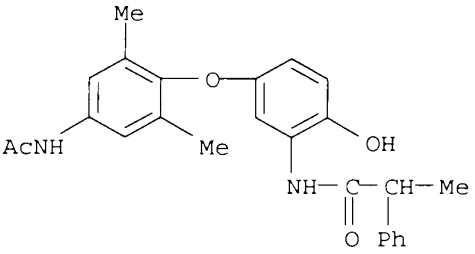
RN 398523-79-0 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxobutyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



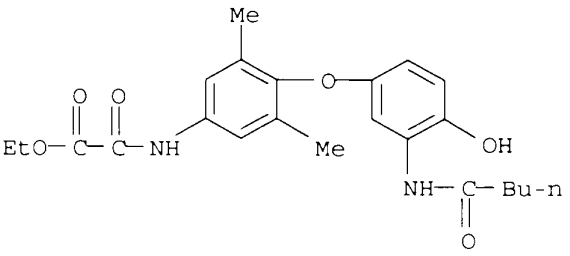
RN 398523-80-3 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(2-methyl-1-oxopropyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



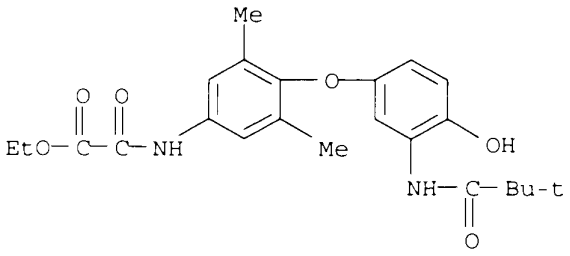
RN 398523-82-5 CAPLUS
CN Benzeneacetamide, N-[5-[4-(acetylamino)-2,6-dimethylphenoxy]-2-hydroxyphenyl]-.alpha.-methyl- (9CI) (CA INDEX NAME)



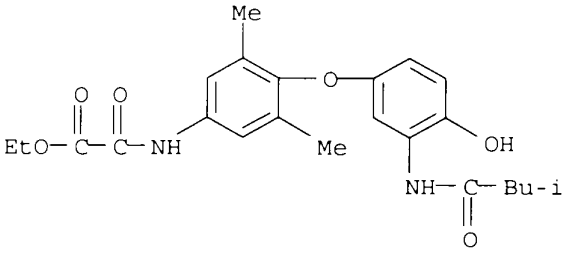
RN 398523-83-6 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxopentyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



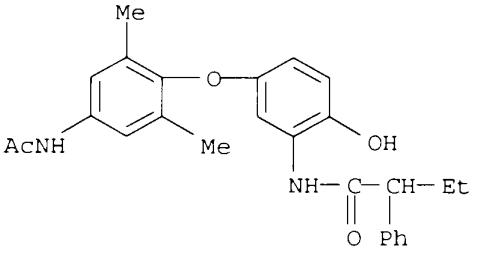
RN 398523-84-7 CAPLUS
CN Acetic acid, [[4-[3-[(2,2-dimethyl-1-oxopropyl)amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



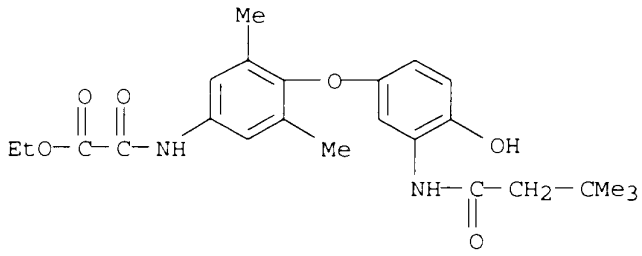
RN 398523-85-8 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(3-methyl-1-oxobutyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



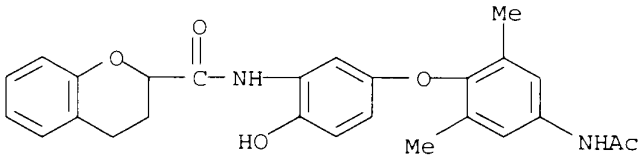
RN 398523-87-0 CAPLUS
CN Benzeneacetamide, N-[5-[4-(acetylamino)-2,6-dimethylphenoxy]-2-hydroxyphenyl]-.alpha.-ethyl- (9CI) (CA INDEX NAME)



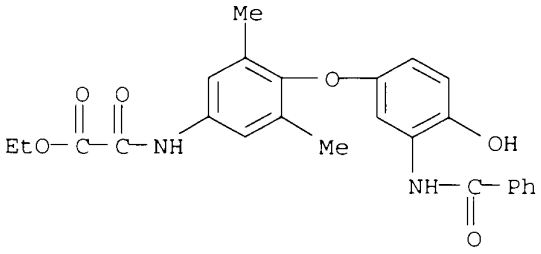
RN 398523-89-2 CAPLUS
CN Acetic acid, [[4-[3-[(3,3-dimethyl-1-oxobutyl)amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



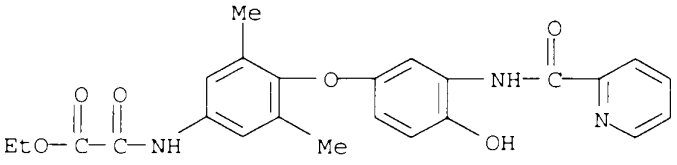
RN 398523-90-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxamide, N-[5-[4-(acetylamino)-2,6-dimethylphenoxy]-2-hydroxyphenyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



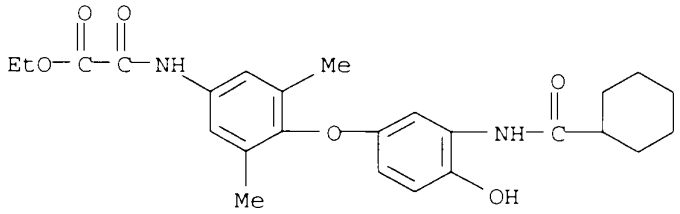
RN 398523-91-6 CAPLUS
CN Acetic acid, [[4-[3-(benzoylamino)-4-hydroxyphenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



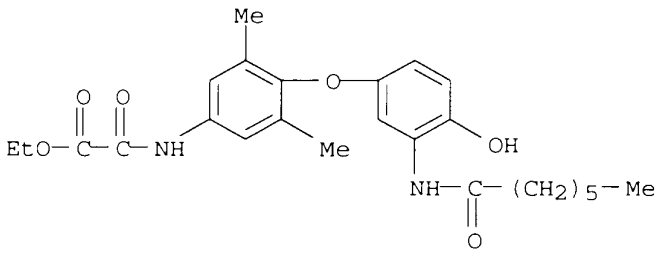
RN 398523-93-8 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(2-pyridinylcarbonyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



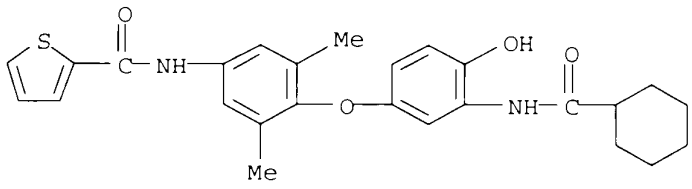
RN 398523-94-9 CAPLUS
CN Acetic acid, [[4-[3-[(cyclohexylcarbonyl)amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



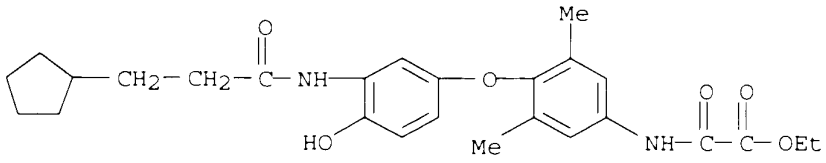
RN 398523-95-0 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxoheptyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 398523-98-3 CAPLUS
CN 2-Thiophenecarboxamide, N-[4-[3-[(cyclohexylcarbonyl)amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]- (9CI) (CA INDEX NAME)

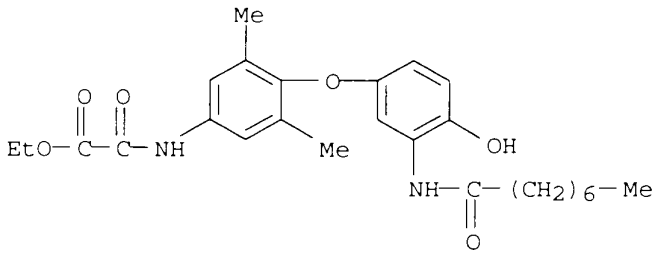


RN 398523-99-4 CAPLUS
CN Acetic acid, [[4-[3-[(3-cyclopentyl-1-oxopropyl)amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)

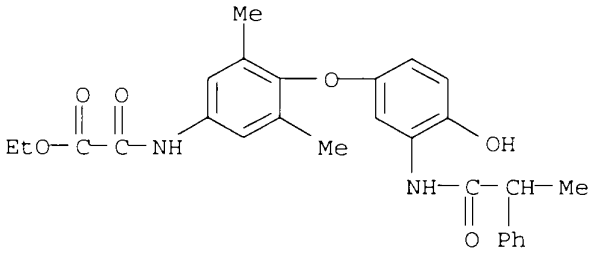


RN 398524-00-0 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxooctyl)amino]phenoxy]-3,5-

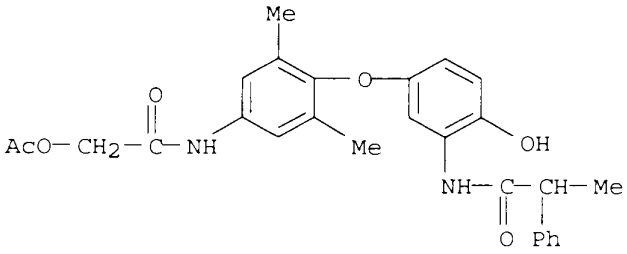
dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



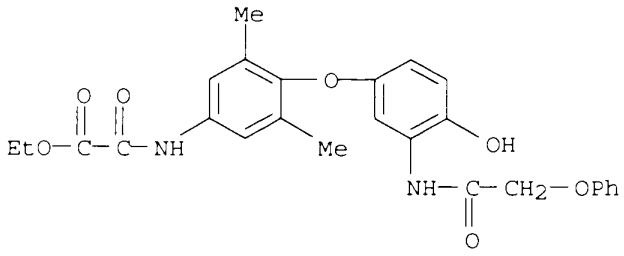
RN 398524-01-1 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxo-2-phenylpropyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



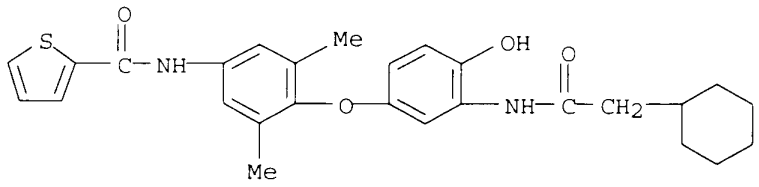
RN 398524-02-2 CAPLUS
CN Benzeneacetamide, N-[5-[4-[[(acetyloxy)acetyl]amino]-2,6-dimethylphenoxy]-2-hydroxyphenyl]-.alpha.-methyl- (9CI) (CA INDEX NAME)



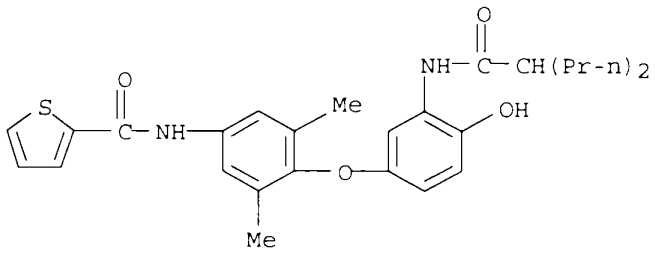
RN 398524-03-3 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(phenoxyacetyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



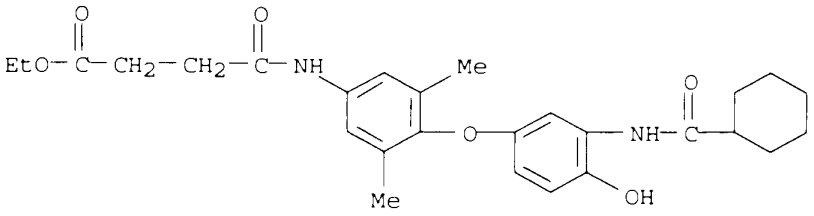
RN 398524-04-4 CAPLUS
CN 2-Thiophenecarboxamide, N-[4-[3-[(cyclohexylacetyl)amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]- (9CI) (CA INDEX NAME)



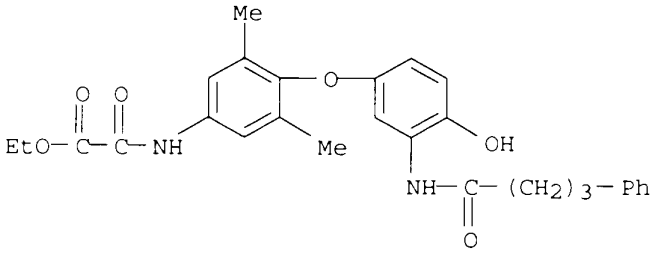
RN 398524-05-5 CAPLUS
CN 2-Thiophenecarboxamide, N-[4-[4-hydroxy-3-[(1-oxo-2-propylpentyl)amino]phenoxy]-3,5-dimethylphenyl]- (9CI) (CA INDEX NAME)



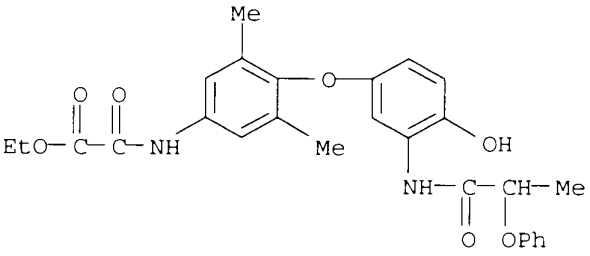
RN 398524-06-6 CAPLUS
CN Butanoic acid, 4-[[4-[3-[(cyclohexylcarbonyl)amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]amino]-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



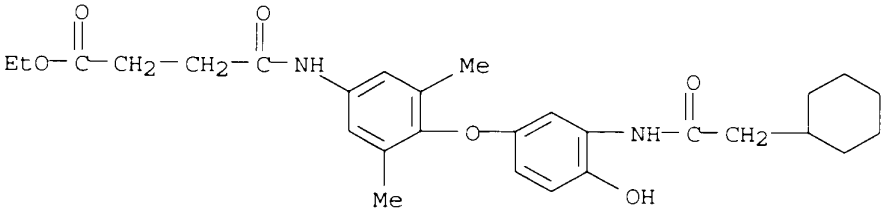
RN 398524-09-9 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxo-4-phenylbutyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



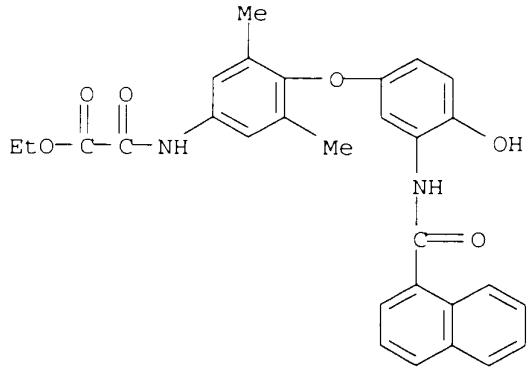
RN 398524-11-3 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxo-2-phenoxypropyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



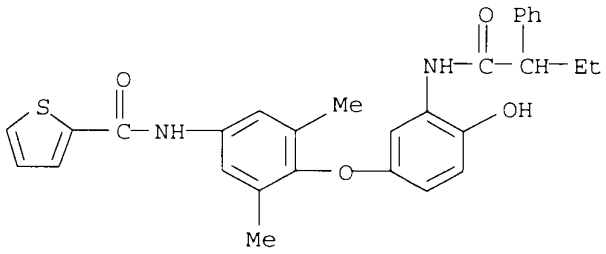
RN 398524-12-4 CAPLUS
CN Butanoic acid, 4-[[4-[3-[(cyclohexylacetyl)amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]amino]-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



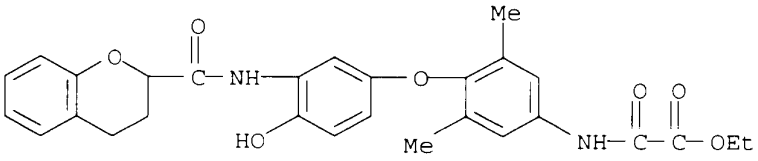
RN 398524-13-5 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-naphthalenylcarbonyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



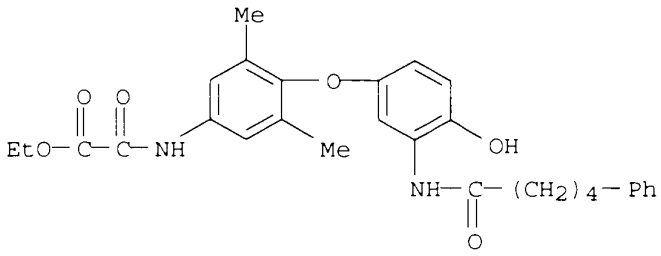
RN 398524-15-7 CAPLUS
CN 2-Thiophenecarboxamide, N-[4-[4-hydroxy-3-[(1-oxo-2-phenylbutyl)amino]phenoxy]-3,5-dimethylphenyl]- (9CI) (CA INDEX NAME)



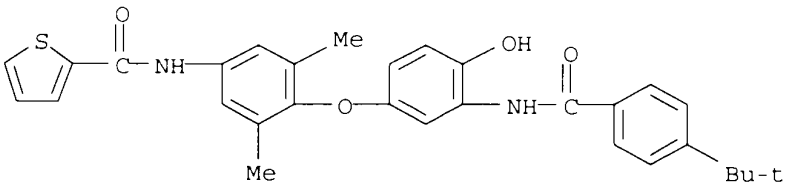
RN 398524-17-9 CAPLUS
CN Acetic acid, [[4-[3-[[(3,4-dihydro-2H-1-benzopyran-2-yl)carbonyl]amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



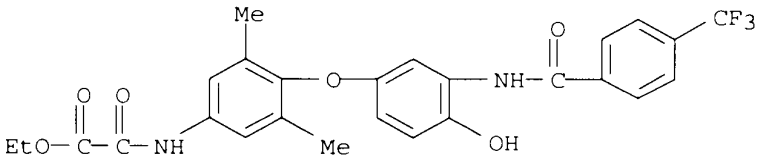
RN 398524-18-0 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[(1-oxo-5-phenylpentyl)amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



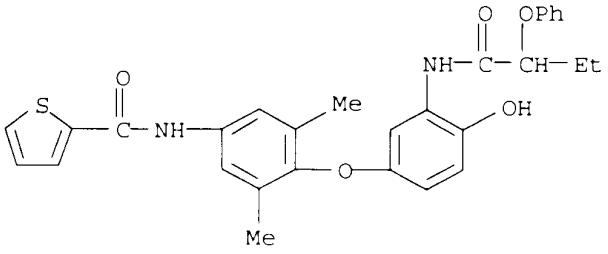
RN 398524-19-1 CAPLUS
CN 2-Thiophenecarboxamide, N-[4-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]- (9CI) (CA INDEX NAME)



RN 398524-20-4 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[[4-(trifluoromethyl)benzoyl]amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)

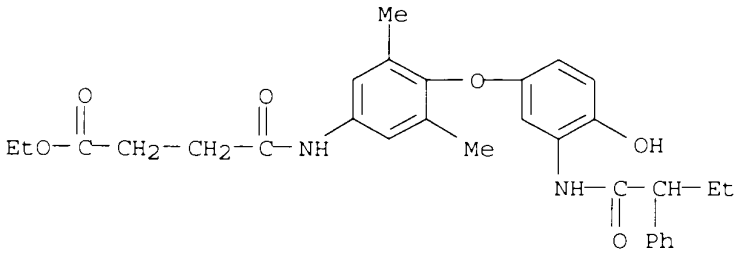


RN 398524-21-5 CAPLUS
CN 2-Thiophenecarboxamide, N-[4-[4-hydroxy-3-[(1-oxo-2-phenoxybutyl)amino]phenoxy]-3,5-dimethylphenyl]- (9CI) (CA INDEX NAME)

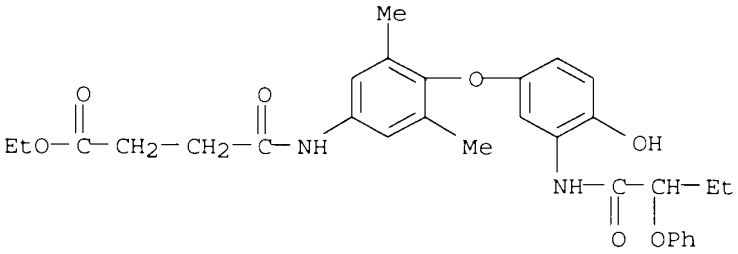


RN 398524-22-6 CAPLUS
CN Butanoic acid, 4-[[4-[4-hydroxy-3-[(1-oxo-2-phenylbutyl)amino]phenoxy]-3,5-

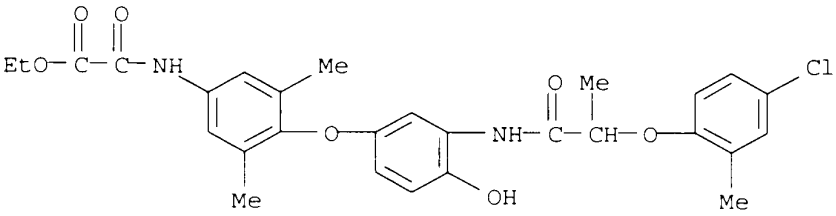
dimethylphenyl]amino]-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



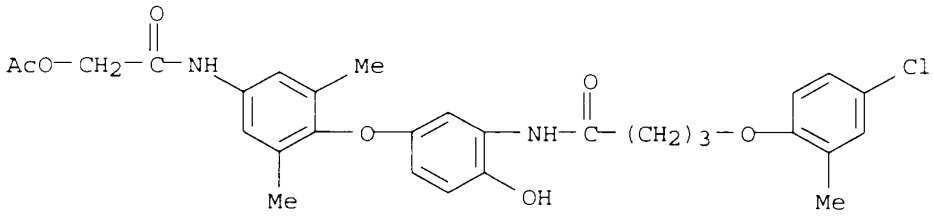
RN 398524-24-8 CAPLUS
CN Butanoic acid, 4-[[4-[4-hydroxy-3-[(1-oxo-2-phenoxybutyl)amino]phenoxy]-3,5-dimethylphenyl]amino]-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



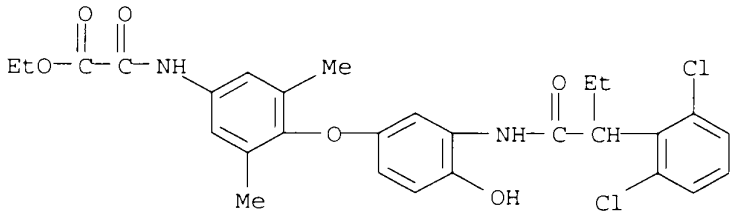
RN 398524-26-0 CAPLUS
CN Acetic acid, [[4-[3-[[2-(4-chloro-2-methylphenoxy)-1-oxopropyl]amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



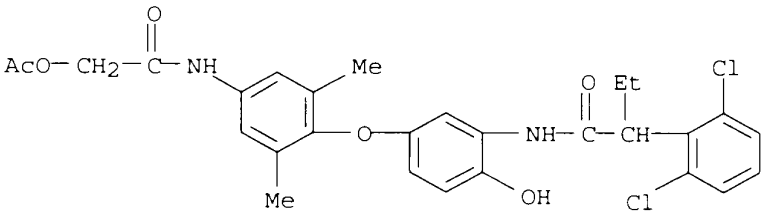
RN 398524-28-2 CAPLUS
CN Butanamide, N-[5-[4-[[(acetyloxy)acetyl]amino]-2,6-dimethylphenoxy]-2-hydroxyphenyl]-4-(4-chloro-2-methylphenoxy)- (9CI) (CA INDEX NAME)



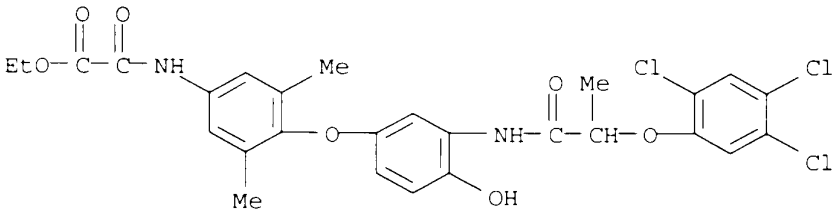
RN 398524-29-3 CAPLUS
CN Acetic acid, [[4-[3-[[2-(2,6-dichlorophenyl)-1-oxobutyl]amino]-4-hydroxyphenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



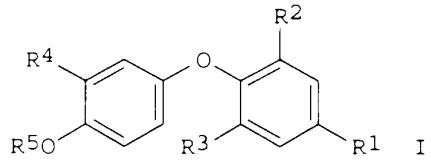
RN 398524-30-6 CAPLUS
CN Benzeneacetamide, N-[5-[4-[[(acetyloxy)acetyl]amino]-2,6-dimethylphenoxy]-2-hydroxyphenyl]-2,6-dichloro-.alpha.-ethyl- (9CI) (CA INDEX NAME)



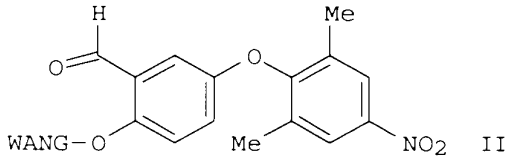
RN 398524-35-1 CAPLUS
CN Acetic acid, [[4-[4-hydroxy-3-[[1-oxo-2-(2,4,5-trichlorophenoxy)propyl]amino]phenoxy]-3,5-dimethylphenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



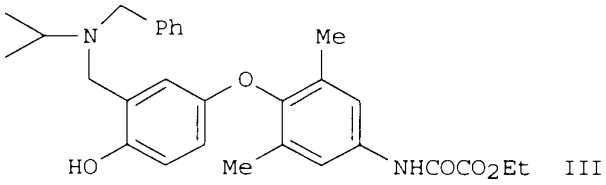
GI



I



II

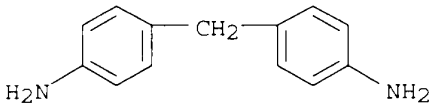


III

AB Title compds. [I; R1 = NO2, amino, acetamido, NHCOCOA, NHCH2COA; A = OH, alkoxy; R2, R3 = halo, alkyl, CF3; R4 = ENR6R7, ENR9COR8, NHCOR10, CONR11R12; E = alkylene; R6, R7 = (substituted) alkyl, aryl, cycloalkyl, heterocyclyl; R6R7N = heterocyclyl; R8 = (substituted) alkyl, cycloalkyl, aryl, biphenyl, alkoxy; R9 = (substituted) alkyl optionally interrupted by O, cycloalkyl, alkenyl, Ph, pyridyl; R8R9 = atoms to form a 4-7 membered heterocyclyl; R10 = (substituted) alkyl, cycloalkyl, aryl, 5-6 membered (arom.), (benzoannellated) heterocyclyl; R11, R12 = H, (substituted) alkyl, cycloalkyl, 5-7 membered heterocyclyl; R11R12N = 5-7 membered (benzoannellated) (substituted) (arom.) heterocyclyl], were prepd. Thus, resin-bound substrate (II) was converted to title compd. (III) in several steps using isopropylamine, benzyl chloride, and ethoxalyl chloride. Tested I showed T3 thyroid hormone receptor promoter activity with EC50 = 2.4-55 nM.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

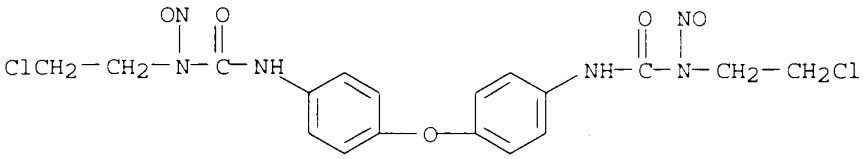
L4 ANSWER 34 OF 54 CAPLUS COPYRIGHT 2003 ACS
AN 2002:101799 CAPLUS
DN 136:295464
TI Free Volume and Transport Properties in Highly Selective Polymer Membranes
AU Nagel, C.; Guenther-Schade, K.; Fritsch, D.; Strunskus, T.; Faupel, F.
CS Technische Fakultaet, Lehrstuhl fuer Materialverbunde, Christian-Albrechts-Universitaet zu Kiel, Kiel, D-24143, Germany
SO Macromolecules (2002), 35(6), 2071-2077
CODEN: MAMOBX; ISSN: 0024-9297
PB American Chemical Society
DT Journal
LA English



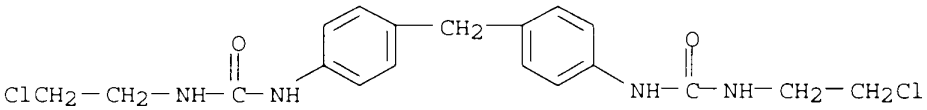
● 2 HCl

AB The carcinogenicity of 35 compds. was evaluated in young female rats 9 months after the oral feeding of 10 equal doses (at 3-day intervals) at the maximally tolerated level. The following compds. caused breast **cancer** (total dose given): 2-anthramine (25 mg.), 2,7-fluorenediamine (400 mg.), benzidine (50 mg.), N-6-benzocoumarinyl)acetamide (1000 mg.), [.alpha.-(2-methylhydrazino)toluoyl]urea-HBr (100 mg.), and 7,12-dimethylbenz[a]anthracene (18 mg.). Weaker responses were elicited by tolidine (500 mg.), 4,4'-thiodianiline (400 mg.), and 1-chloro-2,4-dinitronaphthalene (3000 mg.). 3,3',4,4'-Biphenyltetramine (1000 mg.), 1,3,7-tribromo-2-fluorenamine (20 mg.), 1-anthramine (800 mg.), and nitrofurazone (500 mg.) led to a borderline response. 2-Aminoanthraquinone (1000 mg.) induced cystic changes in the kidneys in most of the treated rats. Various compds. induced single lesions at sites other than the breasts. Multiple dosing was no more effective than single large doses for pinpointing active compds. Mammary **cancer** induction in young female rats is a rapid and sensitive technique for detection of the carcinogenicity of polynuclear aromatic hydrocarbons, polycyclic nitro derivs., polycyclic amino derivs., and select heterocyclic compds. 40 references.

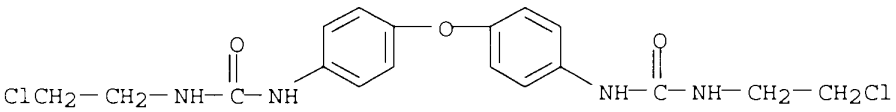
L8 ANSWER 98 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1967:1279 CAPLUS
DN 66:1279
TI Synthesis of potential anticancer agents. XXXVI. N-nitrosoureas. 2. Haloalkyl derivatives
AU Johnston, Thomas Patrick; McCaleb, George S.; Opliger, Pamela S.; Montgomery, John A.
CS Kettering-Meyer Lab., Southern Res. Inst., Birmingham, AL, USA
SO Journal of Medicinal Chemistry (1966), 9(6), 892-910
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
IT **13907-63-6 13908-71-9 13908-72-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as neoplasm inhibitor)
RN 13907-63-6 CAPLUS
CN Urea, 1,1'-(oxydi-p-phenylene)bis[3-(2-chloroethyl)-3-nitroso- (8CI) (CA INDEX NAME)



RN 13908-71-9 CAPLUS
CN Urea, 1,1'-(methylenedi-p-phenylene)bis[3-(2-chloroethyl)- (8CI) (CA INDEX NAME)



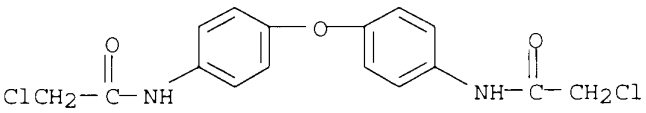
RN 13908-72-0 CAPLUS
CN Urea, 1,1'-(oxydi-p-phenylene)bis[3-(2-chloroethyl)- (8CI) (CA INDEX NAME)



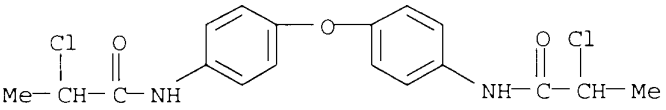
AB cf. CA 64, 11240d. The synthesis, chem. properties, and structure of numerous congeners of 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU), an exptl. important anticancer agent, were investigated, and structure-activity relations established with respect to intraperitoneally and intracerebrally inoculated L1210 mouse leukemia. Structural modifications include variation of halogen, alkyl branching, and introduction of variation of halogen, alkyl branching, and introduction of variously substituted cycloaliphatic, aromatic, and heterocyclic groups. Decompn. with amines as a method of detg. the position of nitrosation in nitroso derivs. of unsym. 1,3-disubstituted ureas was complemented principally by proton N.M.R. spectroscopy. The effect of steric factors and aq. diln. of the nitrosating medium (HCO2H) on isomer ratios in the nitrosation of 2-(haloethyl)ureas having certain cyclic substituents was demonstrated, as well as relative lability of certain nitrosoureas in undild. HCO2H. The most active nitrosoureas so far evaluated against both the intraperitoneal and intracerebral disease are 1-[2-(chloro or fluoro)ethyl]-1-nitrosoureas substituted in the 3-position by a 2-(chloro or fluoro)-ethyl or cycloaliphatic group. A few exceptions to this generalization were noted. 55 references.

L8 ANSWER 99 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1966:499133 CAPLUS
DN 65:99133
OREF 65:18523b-c
TI Potential anticancer compounds. 2-Carbamoyl and 2-phenyl carbamoyl derivatives of 1,3-cyclohexanedione-type compounds
AU Papadakis, Philippos E.; Haven, Guy
CS Veterans Admin. Hosp., Omaha, NE

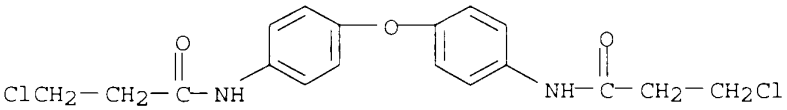
SO Journal of Pharmaceutical Sciences (1966), 55(10), 1016-20
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
IT **10224-03-0**, Acetanilide, 4',4'''-oxybis[2-chloro-
10224-04-1, Propionanilide, 4',4'''-oxybis[2-chloro-
10224-05-2, Propionanilide, 4',4'''-oxybis[3-chloro-
10224-06-3, Acetanilide, 4',4'''-oxybis[2-bromo-
10224-07-4, Propionanilide, 4',4'''-oxybis[2-bromo-
10224-08-5, Propionanilide, 4',4'''-oxybis[3-bromo-
10224-09-6, Acetanilide, 4',4'''-oxybis[2-iodo- **10224-10-9**
, Propionanilide, 4',4'''-oxybis[3-iodo-
(prepn. of)
RN 10224-03-0 CAPLUS
CN Acetamide, N,N'-(oxydi-4,1-phenylene)bis[2-chloro- (9CI) (CA INDEX NAME)



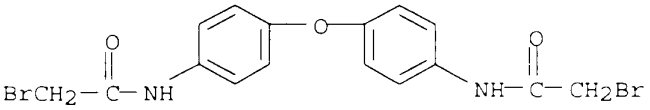
RN 10224-04-1 CAPLUS
CN Propionanilide, 4',4'''-oxybis[2-chloro- (7CI, 8CI) (CA INDEX NAME)



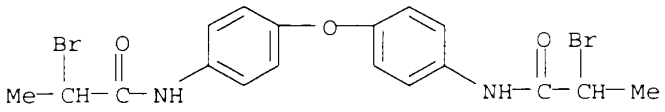
RN 10224-05-2 CAPLUS
CN Propionanilide, 4',4'''-oxybis[3-chloro- (7CI, 8CI) (CA INDEX NAME)



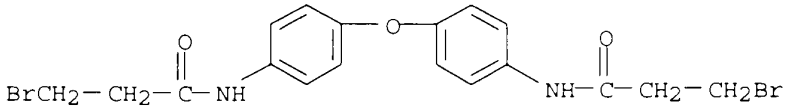
RN 10224-06-3 CAPLUS
CN Acetanilide, 4',4'''-oxybis[2-bromo- (7CI, 8CI) (CA INDEX NAME)



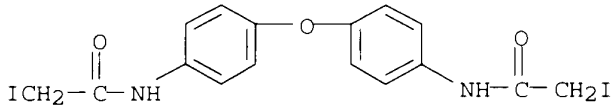
RN 10224-07-4 CAPLUS
CN Propionanilide, 4',4'''-oxybis[2-bromo- (7CI, 8CI) (CA INDEX NAME)



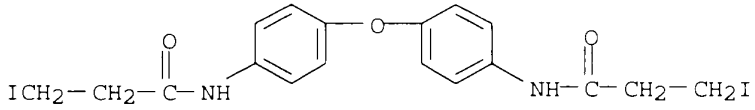
RN 10224-08-5 CAPLUS
CN Propionanilide, 4',4'''-oxybis[3-bromo- (7CI, 8CI) (CA INDEX NAME)



RN 10224-09-6 CAPLUS
CN Acetanilide, 4',4'''-oxybis[2-iodo- (7CI, 8CI) (CA INDEX NAME)

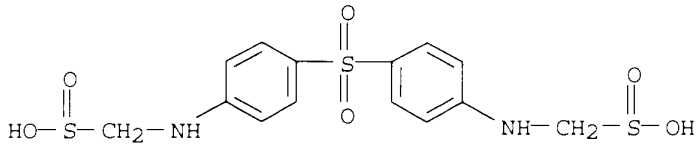


RN 10224-10-9 CAPLUS
CN Propionanilide, 4',4'''-oxybis[3-iodo- (7CI, 8CI) (CA INDEX NAME)



AB 2-Carbamoyl and 2-phenylcarbamoyl derivs. of 1,3-cyclic diketones were prepd. as potential antibacterial and anti-**cancer** reagents.

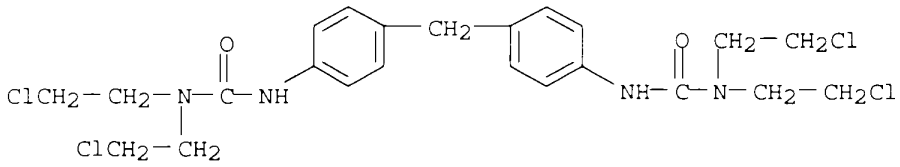
L8 ANSWER 100 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1966:96937 CAPLUS
DN 64:96937
OREF 64:18288d-f
TI On the carcinogenicity of a single intragastric dose of hydrocarbons, nitrosamines, aromatic amines, dyes, coumarins, and miscellaneous chemicals in female Sprague-Dawley rats
AU Griswold, D. P., Jr.; Casey, A. E.; Weisburger, E. K.; Weisburger, J. H.; Schabel, F. M., Jr.
CS Birmingham Baptist Hosp., Birmingham, AL
SO Cancer Res. (1966), 4, 619-25
DT Journal
LA English
IT **144-75-2**, Aniline, 4,4'-sulfonyldi-, bis(sodium formaldehydesulfoxylate)
(as carcinogenic substance)
RN 144-75-2 CAPLUS
CN Methanesulfinic acid, [sulfonylbis(4,1-phenyleneimino)]bis-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

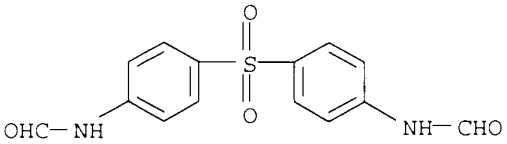
AB The carcinogenic activity of 50 compds. was detd. in rats 6 months following the oral administration of a single dose of each compd. **Cancer** of the breast was observed in rats receiving a max. tolerated dose of 7,12-dimethylbenz[a]anthracene, 4H-cyclopenta[def]phenanthrene (I), 2,3-dihydro-3-ethyl-6-methylcyclopenta[a] anthracene, 2-anthramine (II), dimethyl-p-styrylaniline, 4'-fluoro-4-biphenylylamine, N-(7-chloro-2-fluorenyl)acetamide, 2,7-fluorenediamine, 3-methyl-2-naphthylamine-HCl (III), N-hydroxy-N-(2-fluorenyl)acetamide (IV); N-6-(3,4-benzocoumarinyl)acetamide, 5,5-diphenylhydantoin, 1-chloro-2,4-dinitronaphthalene, or p-ureidobenzenearsonic acid. Carcinoma of the kidney was seen in 1 rat of 20 with I, II, III, IV, and 2,4,6-trimethylacetanilide, and Color Index Acid Blue 9 was present in 1 control rat of 89. Carcinoma of the lung was seen in 1 rat fed dinitrochloronaphthalene and in 1 control animal. Precancerous change in the ovary occurred in a rat fed 4,4-sulfonyldianiline and in none of the control animals. To be carcinogenic in this system [the Huggins system], a compd. must possess some selective ability to conc. in, and remain long enough to initiate carcinogenesis in the mammary gland.

L8 ANSWER 101 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1962:60364 CAPLUS
DN 56:60364
OREF 56:11471d-f
TI Synthesis of potential anticancer agents. VI. Urea and thiourea mustards
AU Popp, Frank D.; Swarz, Herbert
CS U.S. Rubber Co., Wayne, NJ
SO J. Org. Chem. (1961), 26, 4764-5
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA Unavailable
IT **100659-83-4**, Urea, 1,1'-(methylenedi-p-phenylene)bis[3,3-bis(2-chloroethyl)-
(prepn. of)
RN 100659-83-4 CAPLUS
CN Urea, 1,1'-(methylenedi-p-phenylene)bis[3,3-bis(2-chloroethyl)- (7CI) (CA INDEX NAME)



AB Ureas and thioureas, RNHC(:X)N(CH2-CH2Cl)2 (I) (X = O or S), were prepd. by adding the iso-cyanate or isothiocyanate and N,N-bis(2-chloroethyl)amine in benzene. The product pptd. or oiled out anal. pure. I (X = O) prepd. were (R and m.p. given): Et, - (oil); o-ClC6H4, 72-5.degree.; m-ClC6H4, 94-5.degree.; p-ClC6H4, 143-5.degree.; p-O2NC6H4, 150-3.degree.; p-MeC6H4, 88-90.degree.; o-MeOC6H4, 99-101.degree.; p-MeOC6H4, 144-5.degree.; 4,3-Me[(ClCH2CH2)2NCO-NH]C6H3, 85-7.degree.; p-[p- (ClCH2CH2)2NCONHC6H4CH2]-C6H4, 107-10.degree.. I (X = S): Et, -- (oil); Bu, -- (oil); Ph, 76-80.degree.; n-C7H15, -- (oil). The ureas had little or no activity for Dunning leukemia and thioureas only moderate activity.

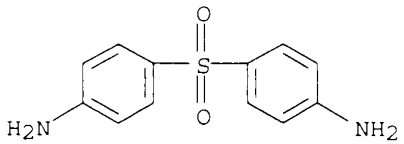
L8 ANSWER 102 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1962:7487 CAPLUS
DN 56:7487
OREF 56:1369a-g
TI Potential cancerocidal agents. III. Formanilides
AU Pettit, George R.; Kalnins, Malda V.; Liu, Thomas M. H.; Thomas, Evan G.; Parent, Kevin
CS Univ. of Maine, Orono
SO J. Org. Chem. (1961), 26, 2563-6
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA Unavailable
IT **6784-25-4**, Formanilide, 4',4'''-sulfonylbis-
(prepn. of)
RN 6784-25-4 CAPLUS
CN Formamide, N,N'-(sulfonyldi-4,1-phenylene)bis- (9CI) (CA INDEX NAME)



AB cf. CA 54, 24754a. Substituted anilides (0.15 mole) in 150 ml. com. HCONMe2 (dried 48 hrs. over Molecular Sieve Type 4A) refluxed 30 min. with 0.3 mole dry freshly prepd. NaOMe with evolution of Me2NH and the mixt. dild. with 300-800 ml. H2O and refrigerated 16 hrs. gave the substituted form-anilide (I). HCONMe2 (150 ml.) contg. 12.1 g. 2,5(MeO)2-C6H3NH2 treated (N atm.) with 6.8 g. 53% NaH in mineral oil and the mixt. refluxed 20 min., cooled (ice bath), decompd. with H2O, dild. to 1 l. with H2O, and refrigerated 16 hrs. gave 10.3 g. 2,5-(MeO)2C6H3NHCHO. Data for I are tabulated [substituents, % yield, and m.p. (solvent) given]: 2-Et, 97, 73.5-4.5.degree. (EtOH-H2O); 2-MeO, 44, 84.degree. (Et-OH-H2O); 4-MeO, 41, 80-1.degree.; 2-F, 70, 44.degree. (C6H6-petr. ether); 3-F, 35, 63-4.degree. (C6H6-petr. ether); 4-F, 78, 67-8.degree. (C6H6-petr. ether);

3-CF3, 52, 54-5.degree. (CHCl3-petr. ether); 3-Cl, 48, 56.0-7.5.degree. (MeOH); 4-Cl, 79, 102.0-3.5.degree. (Me2CO); 2-I, 68, 113.0-13.5.degree. (MeOH); 2,3-Me2, 62, 103.5-4.5.degree. (CCl4); 2,4-Me(MeO), 63, 104-5.degree. (MeOH-H2O); 2,4-(MeO)2, 35, 140-1.degree. (EtOH); 2,5-(MeO)2, 48, 79-80.degree. (CCl4); 2,5-(ETO)2, 36, 95.5-6.0.degree. (EtOH-H2O); 3,4-FMe, 53, 68-9.degree. (C6H6-petr. ether); 2,5-MeF, 56, 88-9.degree. (C6H6-petr. ether); 2,4-FMe, 41, 91-2.degree. (C6H6-petr. ether); 3,4-ClF, 73, 94-5.degree. (C6H6-petr. ether); 3,5-(CF3)2, 54, 124-5.degree. (EtOH-H2O); 4,3-Cl(CF3), 58, 108-9.degree. (C6H6-petr. ether); 2,5-Cl(CF3), 35, 110-11.degree. (alc.); 3,4-ClMe, 68.5, 97.0-7.5.degree. (MeOH); 5,2-ClMe, 93, 134.0-4.5.degree. (MeOH); 2,6-ClMe, 79, 167.5-8.0.degree. (MeOH-H2O); 2,3-Cl2, 42, 151.degree. (EtOH- H2O); 3,4-Cl2, 71, 109.5-10.0.degree. (C6H6-CCl4); 2,5-Cl2, 40, 148.degree. (EtOH-H2O); 3,5-Cl2, 54, 130.degree. (EtOH-H2O); 2,6-Br2, 86, 199.5-201.0.degree. (EtOH-H2O); 3,4-Br2, 95, 132-3.degree. (C6H6); 4,2,5-Cl(OMe)2, 108-9.degree. (C6H6-CCl4); 4,2,5-Cl-(OMe)2, 89, 103-4.degree. (EtOH-H2O); 5,2,4-Cl(OMe)2, 76, 184-5.degree. (EtOH); 2,4,5-Cl3, 56, 169.0-9.5.degree. (MeOH-H2O). The HCONMe2-NaOMe reaction was readily extended. Acylation of 27.6 g. p-H2NC6H4NHPh and crystn. of the product from MeOH-H2O yielded 59% material, m. 170-1.degree., recrystd. from MeOH-H2O (Norit) to give p-PhNHC6H4-NHCHO, m. 174.5-5.0.degree.. Conversion of 40 g. p-H2NC6H4SO2C6H4NH2-p gave 48 g. light brown diformyl deriv., m. 242-50.degree., recrystd. from MeOH-H2O (Darco) to give 4,4'-diformamidodiphenyl sulfone, m. 273.0-3.5.degree.. Acylation of 20 g. .alpha.-C10H7NH2 yielded 82.5% formamide deriv., m. 131-5.degree., recrystd. from C6H6 (Norit A) to give 79.5% .alpha.-formamidonaphthalene, m. 138.5-9.5.degree.. Formylation of 10 g. 8,2-H2NC10H6OH and acidification of the cooled mixt. to pH 5 with HCl yielded 73% formamide, recrystd. twice from MeOH-H2O (Darco) to give 2,8-HOC10H6NHCHO, m. 205.5-7.0.degree. (decompn.).

L8 ANSWER 103 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1958:61074 CAPLUS
DN 52:61074
OREF 52:10979c-i,10980a-f
TI Oxidation of aromatic amines. VI. Persulfate oxidation of carcinogenic aromatic amines
AU Sims, Peter
CS Chester Beatty Research Inst., London
SO J. Chem. Soc. (1958) 44-7
DT Journal
LA Unavailable
IT **80-08-0**, Aniline, 4,4'-sulfonyldi-
(oxidn. with alkali peroxydisulfates)
RN 80-08-0 CAPLUS
CN Benzenamine, 4,4'-sulfonylbis- (9CI) (CA INDEX NAME)

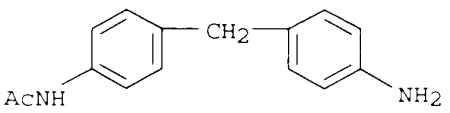


AB cf. C.A. 52, 10028h. Treatment of carcinogenic aromatic amines with alkali persulfates and acid hydrolysis of the intermediate esters gave

.omicron.-aminophenols, some of which were carcinogenic. Aminostilbenes [prepd. according to Haddow, et al. (C.A. 42, 8314e)], 2-Me2NC10H7 (I), m. 46.degree., and 4-Me2NC6H4Ph (II), m. 120.degree. (alc.) (prepd. by the method of Billman, et al., C.A. 37, 13971), and commercially available amines were used. The amines in dil. Me2CO treated with 10% excess Na2S2O8 or K2S2O8 in 20% excess aq. NaOH or KOH as previously described (C.A. 49, 3878h) (solid persulfate added in the beginning of oxidations of tertiary amines) and stirred 8 hrs. at 20.degree., kept overnight and filtered gave solns. worked up as described. The soln. from oxidation of 10 g. 2'-chloro-4-dimethylamino-trans-stilbene (III) evapd. to 200 ml. in vacuo and filtered from 5.2 g. unchanged amine, the filtrate extd. 4 hrs. with Et2O and the aq. phase evapd. to 25 ml. in vacuo, filtered, and the residue recrystd. (H2O) gave the sulfuric ester Na salt. The filtrate acidified with 2N H2SO4 and extd. 3 times with 100 ml. Et2O, the soln. extd. twice with 5 ml. aq. NaHCO3 and the Et2O-washed alk. ext. acidified with 2N H2SO4, the acid soln. kept overnight at 0.degree., filtered, and the product (23 mg.) crystd. (H2O) yielded p-Me2NC6H4CO2H, m. 232-3.degree.. The filtrate extd. 3 times with 50 ml. Et2O and the Et2O evapd., the gummy residue extd. with boiling ligroine and the product (230 mg.) recrystd. 3 times (H2O) gave .omicron.-ClC6H4CO2H, m. 139-40.degree.. The Na salt in H2O acidified with concd. HCl produced 2-chloro-4-dimethylamino-3-hydroxy-trans-stilbene sulfuric ester, m. 220-4.degree. (decompn.) (dil. alc.), bright blue fluorescence in ultraviolet light. The ester (2 g.) in 50 ml. H2O heated 30 min. at 100.degree. with 10 ml. concd. HCl and the cooled soln. treated with a slight excess of aq. NaHCO3 gave 1.25 g. 2'-chloro-4-dimethylamino-3-hydroxy-trans-stilbene, m. 137-8.degree. (dil. alc. or EtOAc), sublimed at 120-70.degree./0.2 to plates, m. 139-9.5.degree., bright blue fluorescence in ultraviolet light. Similar treatment of 10 g. 4-dimethylamino-2'-methyl-trans-stilbene (IIIa) gave 4.9 g. unchanged amine and 3.6 g. Na salt, converted in 25 ml. H2O by acidification with 10N H2SO4 to yield 3.2 g. 4-dimethylamino-3-hydroxy-2'-methyl-trans-stilbene sulfuric ester, m. 183-5.degree. (dil. alc.), bright blue fluorescence. The oxidation of mother liquors gave 165 mg. .omicron.-MeC6H4CO2H, m. 101-2.degree.. The ester (2 g.) hydrolyzed with concd. HCl yielded 1.3 g. 4-dimethylamino-3-hydroxy-2'-methyl-trans-stilbene, m. 153.5-4.5.degree. (dil. alc.), sublimed at 130.degree./10.2, plates, m. 153.5-4.5.degree., strong blue fluorescence in soln. in ultraviolet light. Oxidation of 10 g. 4-Me2NC6H4N2Ph and working up yielded 510 mg. K salt, acidified with HCl to the sulfuric ester, m. 195-8.degree. (dil. alc.), hydrolyzed with HCl to give 3,4-HO(Me2N)C6H3N2Ph (IV), m. 131-1.5.degree.. II (10 g.) oxidized with Na2S2O8 and worked up gave 3.3 g. Na 4-dimethylamino-3-biphenylyl sulfate, acidified in H2O with concd. HCl to yield 4-dimethylamino-3-biphenylyl H sulfate, m. 228-31.degree. (decompn.) (alc.), and hydrolyzed as above (1.2 g.) to give 0.85 g. 3,4-HO(Me2N)C6H3Ph (V), m. 128-9.degree. (dil. alc.). 1-Me2NC10H7 (10 g.) oxidized and the mixt. evapd. to 200 ml. in vacuo, the concentrate washed with Et2O and the aq. soln. adjusted to pH 4 with 2N H2SO4, the acid soln. washed with Et2O and the gummy product (2.9 g.) purified through the Na salt gave 1-dimethylamino-2-naphthyl H sulfate, m. 155-8.degree., hydrolyzed with HCl and the hydrolyzate treated with a slight excess of NaHCO3, the product isolated with Et2O and crystd. (dil. alc.) gave 2,1-HO(Me2N)C10H6 (VI), m. 52-3.degree.; Bz deriv., m. 70-1.degree. (dil. alc.). Similarly, 10 g. I gave 3.7 g. 2-dimethylamino-1-naphthyl H sulfate, m. 172-4.degree., hydrolyzed to a solid, sublimed at 65.degree./0.1 to 1,2-HO(Me2N)C10H6, m. 33-4.degree., rapidly decompd. on exposure to air; Bz deriv., m. 111-13.degree. (ligroine). The residue from oxidation of 10 g. 3,4,1-xylidine extd. 3 times with 100 ml. boiling MeOH and the concd. ext. kept overnight at room

temp., the 4.2 g. Na 2-amino-4,5-dimethylphenyl sulfate in H2O acidified to give the acid sulfate, m. 254-7.degree. (decompn.) (alc.), and the ester (2 g.) hydrolyzed with acid yielded 1.35 g. 4,5,2-Me2(H2N)C6H2OH (VII), m. 169-71.degree. (Et2O), sublimed at 170.degree./0.2 to plates, m. 174-5.degree., reddening in air. p-H2NC6H4SO2NH2 (10 g.) oxidized with K2S2O8 and the mixt. evapd. to 200 ml. in vacuo, the filtered concentrate washed with Et2O and acidified to pH 3 with 2N H2SO4, filtered and the filtrate adjusted to pH 7 with 2N KOH, evapd. in vacuo and the residue extd. 5 times with 100 ml. boiling MeOH, the exts. evapd. and the residue in H2O filtered through a 5 .times. 25 cm. De-Acidite E ion exchange resin, the column washed with MeOH and eluted with 1 l. 2N NH4OH, the fraction taken up in 50 ml. boiling MeOH and the cooled soln. dild. with 50 ml. Et2O, filtered from pptd. colored material and dild. with excess Et2O gave 3.75 g. NH4 2-amino-p-sulfamoylphenyl sulfate, converted in H2O with HCl to 2-amino-p-sulfamoylphenyl H sulfate, purified through the Na salt by acidification and crystn. (MeOH-Et2O) to give pink solvated plates, m. 200-2.degree. (decompn.). The ester hydrolyzed with HCl and the soln. neutralized with NaHCO3, extd. 6 hrs. with Et2O and the product crystd. (alc.-CHCl3) (cf. Thorpe and Williams, C.A. 35, 66716) gave 3,4-HO(H2N)C6H3SO2NH2, m. 162-3.degree.; tri-Bz deriv., m. 222.degree. (dil. alc.). Persulfate oxidations of 2-aminofluorene and 4-H2NC6H4C6H4F-4 yielded brown amorphous substances; oxidations of 2-aminoanthracene, -anthraquinone, and -chrysene were unsuccessful. The oxidation of 4-H2NC6H4N2Ph was limited and (4-H2NC6H4)2SO2, 3,2-Me(H2N)C6H4N2C6H3Me2-2, and 2-(ClCH2CH2)2NC10H7, yielded sulfuric esters which did not crystallize. When implanted into the bladders of mice, IV and VII induced **cancer** of the bladder but under the same conditions of V and VI were not carcinogenic. Although 4-H2NC6H4CH:CHPh (IIIb) was not attacked by persulfate both III and IIIa were oxidized. III and IIIa are more active as growth-inhibitors and carcinogens than IIIb and it appears that compds. more susceptible to persulfate oxidation are the more active biologically.

L8 ANSWER 104 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1951:16379 CAPLUS
DN 45:16379
OREF 45:2893h-i,2894a-f
TI Compounds for **cancer** research. V. Radioactive sulfonamides
AU Ray, Francis E.; Soffer, Louis
CS Univ. of Cincinnati, Cincinnati, O.
SO J. Org. Chem. (1950), 15, 1037-42
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA Unavailable
IT **24367-94-0**, p-Acetotoluidide, .alpha.-(p-aminophenyl)-
(prepn. of)
RN 24367-94-0 CAPLUS
CN Acetamide, N-[4-[(4-aminophenyl)methyl]phenyl]- (9CI) (CA INDEX NAME)



AB cf. C.A. 44, 585h. A no. of sulfonamides (I) are prepd. search for a compd. which will localize selectively in tumor tissue. These compds. may

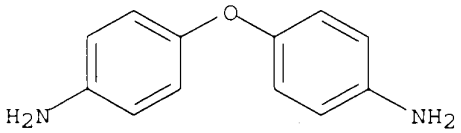
be made radioactive and then serve for diagnostic and therapeutic purposes. PhMe (20 cc.) and 10 cc. H2SO4 contg. 4 millicuries H2S35O4 are heated with stirring within 1 hr. to 195.degree., the mixt. cooled to 100.degree., 3-4 cc. PhMe added, the mixt. heated again in such a way that the H2O formed is collected, the addn. of PhMe and heating repeated 4-5 times until no more H2O is formed, the mixt. heated without reflux to remove the excess PhMe, poured while hot into 100 cc. H2O, neutralized with NaOH, 30 g. NaCl added, and the mixt. heated to dissolve the salt, filtered to remove 2-3 g. (MeC6H4)2SO2, and cooled, giving 19.7-22 g. p-MeC6H4S35O3Na (II). Refluxing 10 g. II with 5 g. PCl5 and 10 cc. POCl3 1.5 hrs. at 160.degree. gives 89.6% p-MeC6H4S35O2Cl (III), m. 69.degree.. Benzidine (6.1 g.) with 14.5 g. III in 20 cc. C5H5N gives 40.6% N,N'-di-p-tosyl-S35-benzidine, large plates, m. 248.degree., with a total of 813,960 c./m. Other I are prepd. with nonradioactive p-MeC6H4SO2Cl (IV) by methods which may be applied to III. p-AcNHC6H4C6H4NH2, m. 199-200.degree. (2.26 g.), with 1.91 g. IV in 10 cc. C5H5N gives 73.8% N-acetyl-N'-p-tosylbenzidine (V), fine needles, m. 227.5.degree.. Refluxing 1 g. V in 25 cc. EtOH and 25 cc. 20% HCl 40 min., distg. off the EtOH in vacuo, and neutralizing the mixt. with NH4OH give 91% N-p-tosylbenzidine, m. 164-5.degree.. (p-H2NC6H4)2S (2.16 g.) with 3.82 g. IV in 15 cc. C5H5N gives 82% (p-MeC6H4SO2NHC6H4)2S, crystals from EtOH, m. 195.degree.. (p-MeC6H4SO2NHC6H4)(p-O2NC6H4)S (VI), 80% yield, m. 157.5-8.5.degree.. Warming 2 g. VI in 20 cc. AcOH with 4.5 g. SnCl2.2H2O in 8 cc. concd. HCl 0.5 hr. at 60.degree. gives 70.4% (p-MeC6H4SO2HNC6H4)(p-H2NC6H4)S, glistening microcrystals, m. 142-3.degree.. Heating 3.96 g. (p-H2NC6H4)CH2 and 7.64 g. IV in 30 cc. C5H5N gives 61% (p-MeC6H4SO2HNC6H4)2CH2, m. 186-7.5.degree.. (p-H2NC6H4)(p-AcHNC6H4)CH2, m. 133-4.degree. (2.4 g.), and 1.9 g. IV in 10 cc. C5H5N 1 hr. at 100.degree. give 82.5% (p-MeC6H4SO2NHC6H4) (p-AcNHC6H4)CH2 (VII), micro needles, m. 167.9-9.2.degree.. Twice was obtained a product, m. 136-7.degree., which does not depress the m.p. of VII and is either a polymorphic form or an adduct with C5H5N. Refluxing 1.97 g. VII with 20 cc. EtOH and 25 cc. 20% HCl gives 79% (p-H2NC6H4) (p-MeC6H4SO2NHC6H4) CH2, m. 156-8.degree.. (p-H2NC6H4)2O (2 g.) and 3.82 g. IV give 71% (p-MeC6H4SO2NHC6H4)2O, m. 179-80.degree.. (p-AcNHC6H4)(p-O2NC6H4)O (1.36 g.), m. 153.degree., prepd. in 28-32% yield from p-HOC6H4NHAc, p-BrC6H4NO2, NaH, and Cu powder, when refluxed 45 min. in 15 cc. EtOH and 25 cc. 20% HCl gives 87% (p-H2NC6H4)(p-O2NC6H4)O, light yellow feathery needles, m. 134-5.degree., 1.33 g. of which, treated 1 hr. at 100.degree. with 0.95 g. IV in 5 cc. C5H5N, gives 75.5% (p-MeC6H4SO2NHC6H4) (p-O2NC6H4)O (VIII), m. 154-5.degree.. Reduction of VIII in AcOH and HCl with SnCl2 gives 77.5% (p-MeC6H4SO2NHC6H4)(p-H2NC6H4) O, needles, m. 141-2.degree., also obtained in a poor yield from (p-H2NC6H4)2O.2HCl, IV, and C5H5N.

L8 ANSWER 105 OF 105 CAPLUS COPYRIGHT 2003 ACS
AN 1948:42486 CAPLUS
DN 42:42486
OREF 42:8931e-h
TI Chemotherapy investigations in **cancer**. Influence of certain organic dibasic acids, diamino compounds and nitro compounds on tumors in mice
AU Woodhouse, D. L.
CS Univ. Birmingham, UK
SO Cancer Research (1947), 7, 398-401
DT Journal
LA Unavailable
IT **101-80-4**, Aniline, 4,4'-oxydi-

(complexes with ribonucleic and desoxyribonucleic acids, effect on tumors)

RN 101-80-4 CAPLUS

CN Benzenamine, 4,4'-oxybis- (9CI) (CA INDEX NAME)



AB The effects have been observed of subcutaneous and intravenous injections of a series of substituted succinic acids on the growth of a dibenzanthracene-induced, transplanted mouse sarcoma, and of subcutaneous injections on benzopyrene-induced papillomas and on carcinoma 63. The effects have been observed of subcutaneous injections of a series of amino compds., and a no. of nucleic acid complexes with these, on mice with carcinoma 63 and dibenzanthracene-induced sarcomas, and the effects have been studied of subcutaneous injections of some nitro org. compds. on these tumors. None of these substances caused complete regression of any of the tumors, but a definite inhibitory effect of the following was observed: methylsuccinic acid, cyclohexylsuccinic acid, cyclohexylacetyl-1-carboxylic acid, malonic acid, 4,4'-diaminodiphenylthiourea, 4,4'-diaminoazobenzene, 4,4'-diaminodiphenyl ether complex with ribonucleic acid, 4,4'-diaminodiphenyl ether complex with desoxyribonucleic acid, and 2-nitrofluorene.